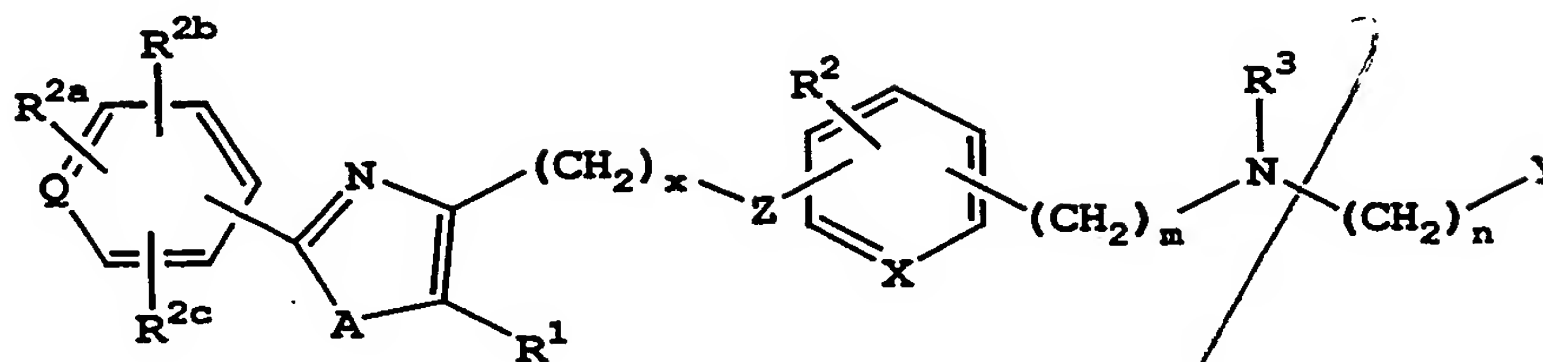


What is Claimed is:

1. A compound which has the structure



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wherein x is 1, 2, 3 or 4; m is 1 or 2; n is 1 or 2;

Q is C or N;

A is 0 or S;

Z is 0 or a bond;

10

R¹ is H or lower alkyl;

X is CH or N;

R² is H, alkyl, alkoxy, halogen, amino or substituted amino;

15 R^{2a} , R^{2b} and R^{2c} are the same or different and are selected from H, alkyl, alkoxy, halogen, amino or substituted amino;

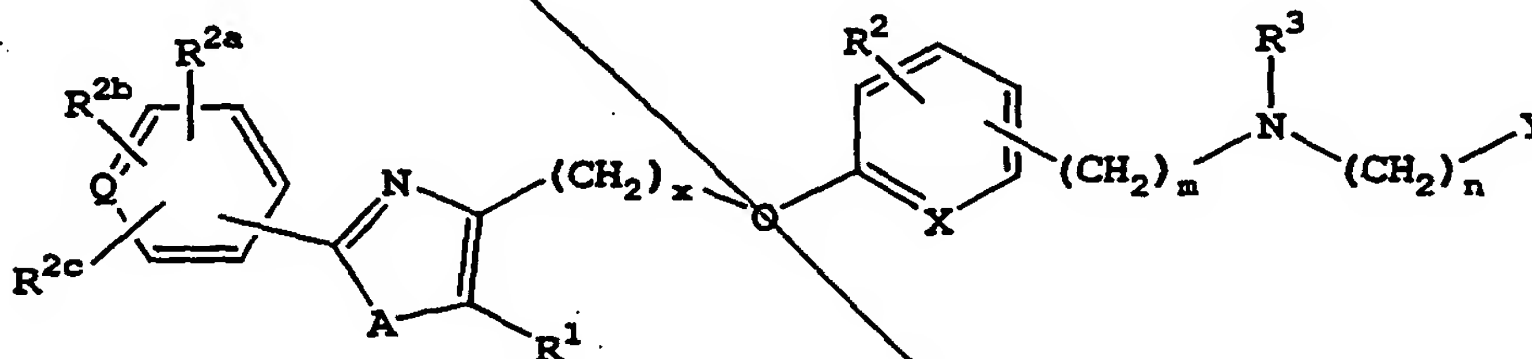
R³ is H, alkyl, arylalkyl, aryloxycarbonyl, alkyloxycarbonyl, alkynyloxycarbonyl, alkenyloxycarbonyl, arylcarbonyl, alkylcarbonyl, aryl, heteroaryl, alkyl(halo)aryloxycarbonyl, alkyloxy(halo)aryloxycarbonyl, cycloalkylaryloxycarbonyl, cycloalkyloxyaryloxycarbonyl, cycloheteroalkyl, heteroarylcarbonyl, heteroaryl-heteroarylalkyl, alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, alkoxycarbonylamino, aryloxycarbonylamino, heteroaryloxycarbonylamino, heteroaryl-heteroarylcarbonyl, alkylsulfonyl, alkenylsulfonyl, heteroaryloxycarbonyl, cycloheteroalkyloxycarbonyl, heteroarylalkyl, aminocarbonyl, substituted aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, heteroarylalkenyl, cycloheteroalkylheteroarylalkyl, hydroxyalkyl, alkoxy, alkoxyaryloxycarbonyl, arylalkyloxycarbonyl, alkylaryloxycarbonyl, arylheteroarylalkyl, arylalkylarylalkyl, aryloxyarylalkyl, alkynyloxycarbonyl,

haloalkoxyaryloxy carbonyl, alkoxycarbonylaryloxy carbonyl,
 aryloxyaryloxy carbonyl, arylsulfinylaryl carbonyl,
 arylthioaryl carbonyl, alkoxycarbonylaryloxy carbonyl,
 arylalkenyloxy carbonyl, heteroaryloxyarylalkyl,
 5 aryloxyaryl carbonyl, aryloxyarylalkyloxy carbonyl,
 arylalkenyloxy carbonyl, arylalkyl carbonyl,
 aryloxyalkyloxy carbonyl arylalkylsulfonyl,
 arylthiocarbonyl, arylalkenylsulfonyl,
 heteroarylsulfonyl, arylsulfonyl, alkoxylarylalkyl,
 10 heteroarylalkoxy carbonyl, arylheteroarylalkyl,
 alkoxylaryl carbonyl, aryloxyheteroarylalkyl,
 heteroarylalkyloxyarylalkyl, arylarylalkyl,
 arylalkenylarylalkyl, arylalkoxyarylalkyl,
 arylcarbonylarylalkyl, alkylaryloxyarylalkyl,
 15 arylalkoxy carbonyl heteroarylalkyl, heteroarylarylalkyl,
 arylcarbonyl heteroarylalkyl, heteroaryloxyarylalkyl,
 arylalkenyl heteroarylalkyl, arylaminoarylalkyl or
 aminocarbonylarylalkyl;

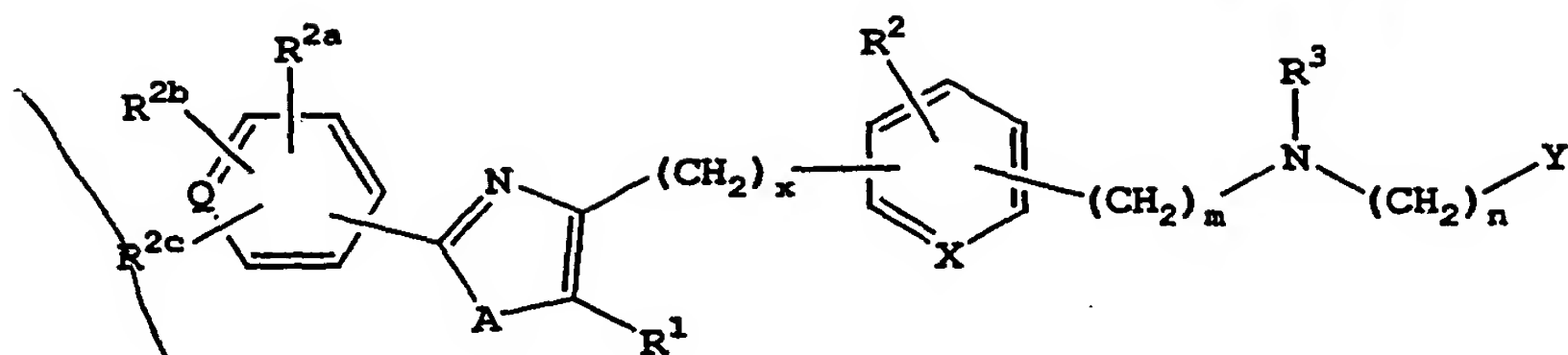
Y is CO_2R^4 (where R^4 is H or alkyl, or a prodrug
 20 ester) or Y is a C-linked 1-tetrazole, a phosphinic acid
 of the structure $\text{P}(\text{O})(\text{OR}^{4a})\text{R}^5$, (where R^{4a} is H or a prodrug
 ester, R^5 is alkyl or aryl) or a phosphonic acid of the
 structure $\text{P}(\text{O})(\text{OR}^{4a})_2$, (where R^{4a} is H or a prodrug ester);
 including all stereoisomers thereof, prodrug
 25 esters thereof, and pharmaceutically acceptable salts
 thereof, with the proviso that where X is CH, A is O, Q
 is C, Z is O and Y is CO_2R^4 , then R^3 is other than H or
 alkyl containing 1 to 5 carbons in the normal chain.

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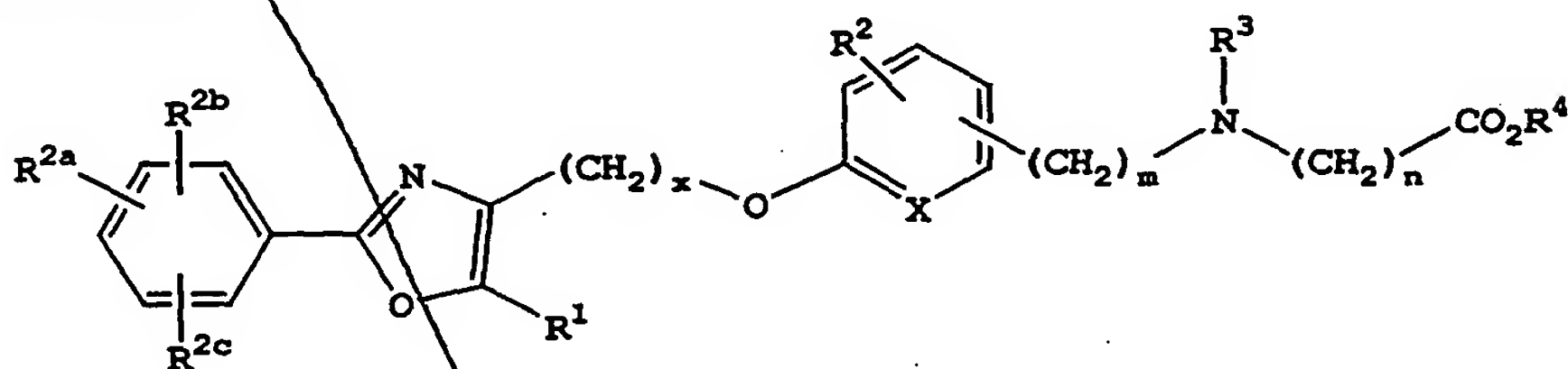
2. A compound having the structure



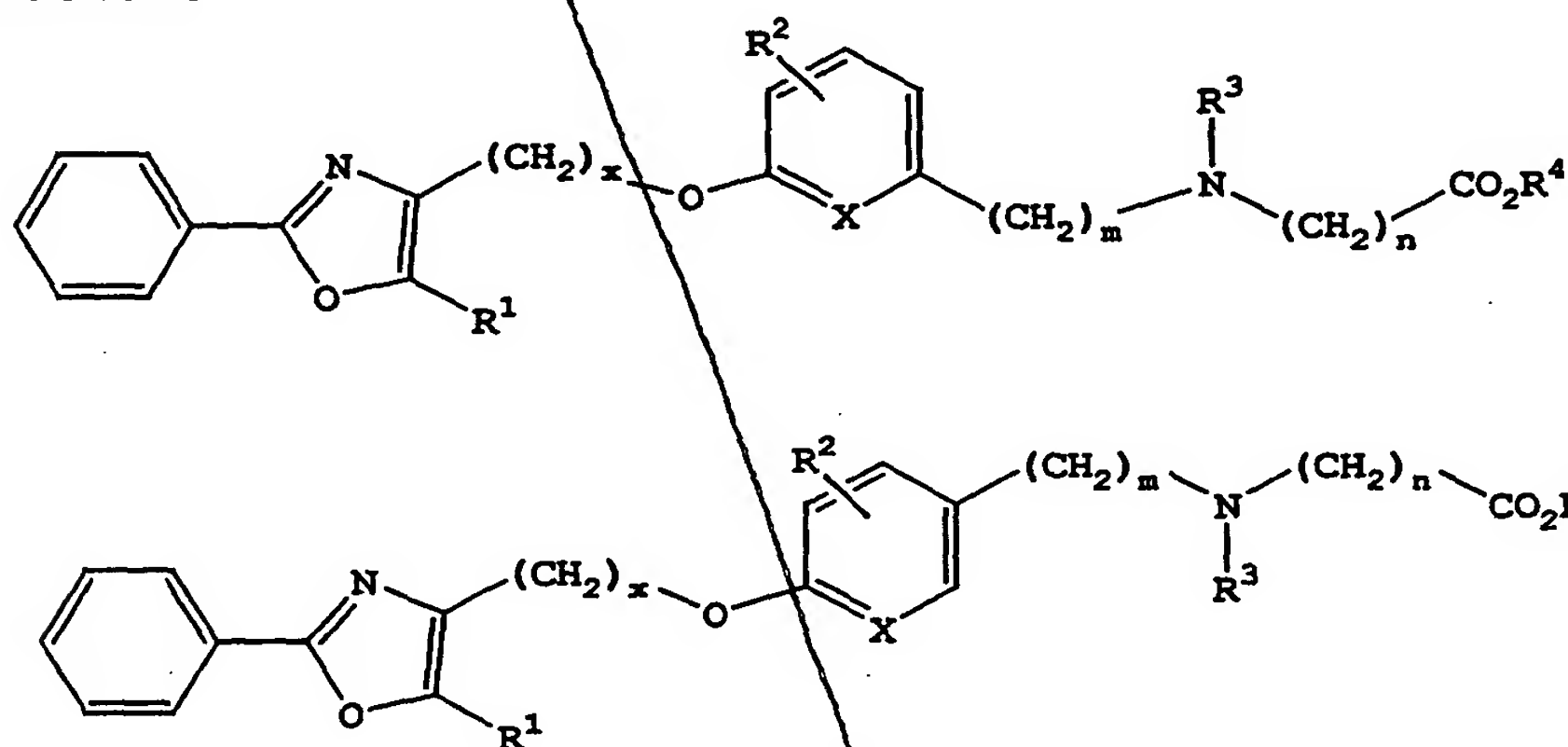
or



3. The compound as defined in Claim 1 having the structure



4. The compound as defined in Claim 1 having structure

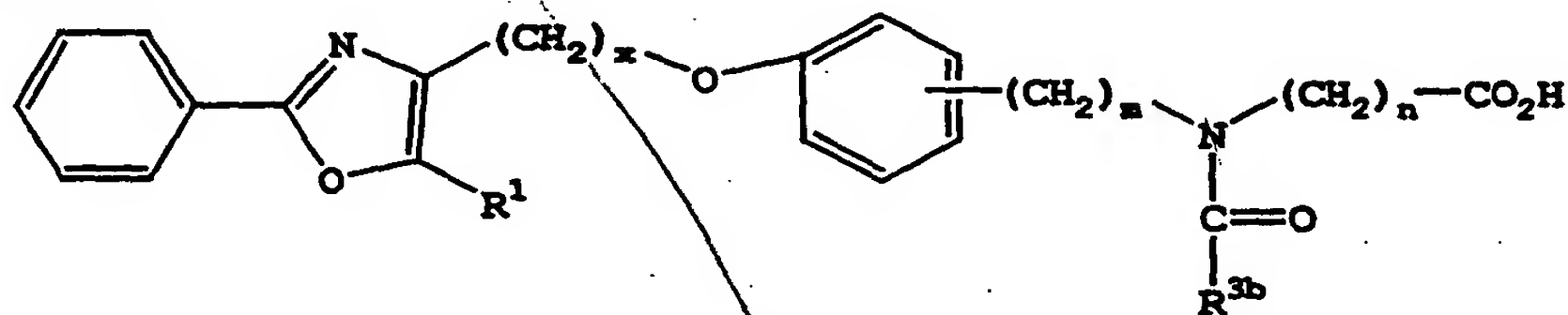


5. The compound as defined in Claim 1 wherein $(CH_2)_x$ is alkylene, alkenylene, allenyl, or alkynylene.

6. The compound as defined in Claim 4 wherein X is CH.

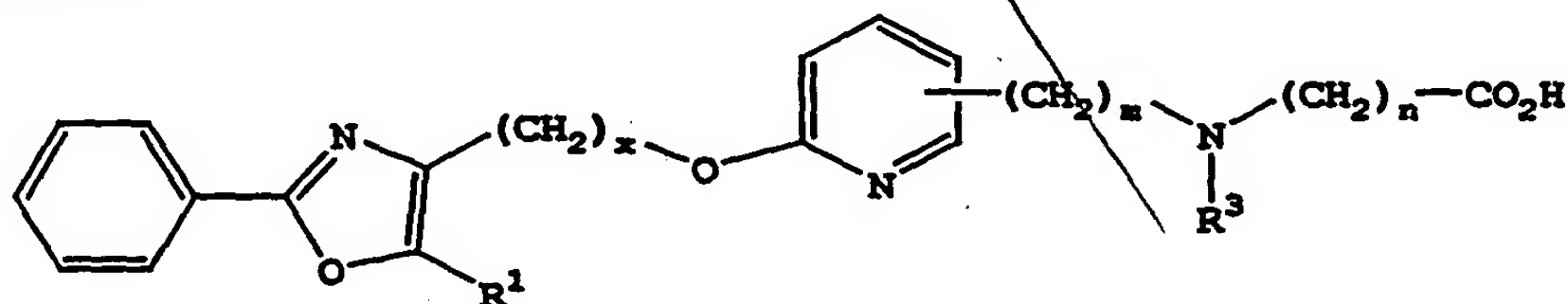
7. The compound as defined in Claim 4 wherein X is N.

8. The compound as defined in Claim 1 having the structure



wherein R^1 is alkyl, R^{3b} is arylalkylamino, aryl-
 5 arylamino, arylamino, alkoxyarylamine, dialkoxyarylamine,
 dihaloarylamine or alkylthioarylamine.

9. The compound as defined in Claim 1 having the structure



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10. The compound as defined in Claim 1 wherein R^{2a} is alkoxy or H,

$(CH_2)_x$ is CH_2 , $(CH_2)_2$, $(CH_2)_3$, or $\begin{array}{c} CH_3 \\ | \\ CH \\ | \\ R_a \end{array}$, $(CH_2)_m$ is CH_2 , or

15 $\begin{array}{c} R_a \\ | \\ CH \end{array}$ (where R_a is alkyl or alkenyl), $(CH_2)_n$ is CH_2 , R^1 is lower alkyl, preferably $-CH_3$, R^2 is H, R^{2a} is H, R^4 is H, X is CH, and R^3 is arylalkyloxycarbonyl, arylheteroarylalkyl, aryloxyarylalkyl, arylalkyl, aryloxycarbonyl, haloaryl-oxycarbonyl,
 20 alkoxyaryloxycarbonyl, alkylaryloxycarbonyl, aryloxyaryloxycarbonyl, heteroaryloxyarylalkyl, heteroaryloxycarbonyl, aryloxyarylcarbonyl, arylalkenyloxycarbonyl, cycloalkylaryloxycarbonyl, arylalkylarylcarbonyl, heteroaryl-heteroarylalkyl,
 25 cycloalkyloxyaryloxycarbonyl, heteroaryl-heteroarylcarbonyl, alkyloxyaryloxycarbonyl, arylalkylsulfonyl, arylalkenylsulfonyl, alkoxyarylalkyl, arylthiocarbonyl, cycloheteroalkylalkyloxycarbonyl, cycloheteroalkyloxycarbonyl, or polyhaloalkylaryloxy-
 30 carbonyl, which may be optionally substituted.

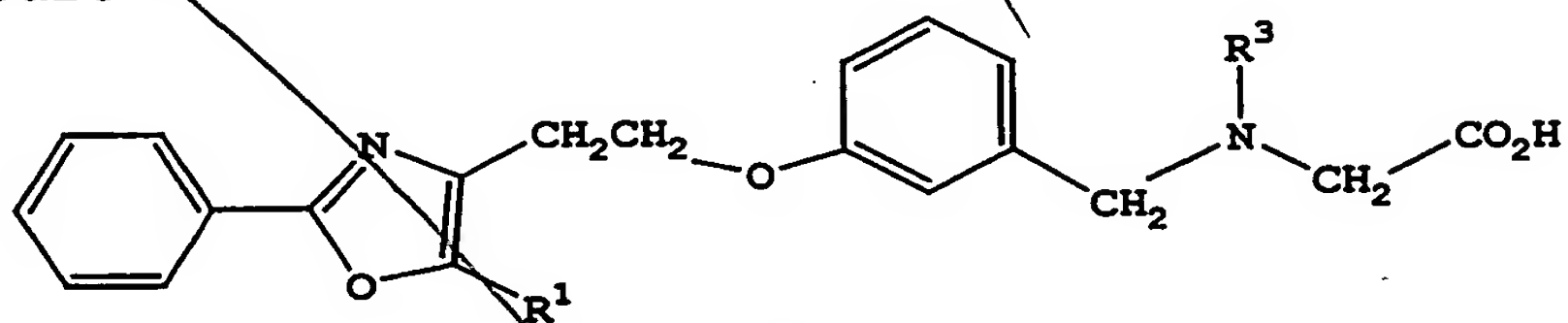
11. The compound as defined in Claim 5 wherein X is CH.

5 12. The compound as defined in Claim 5 wherein X is N.

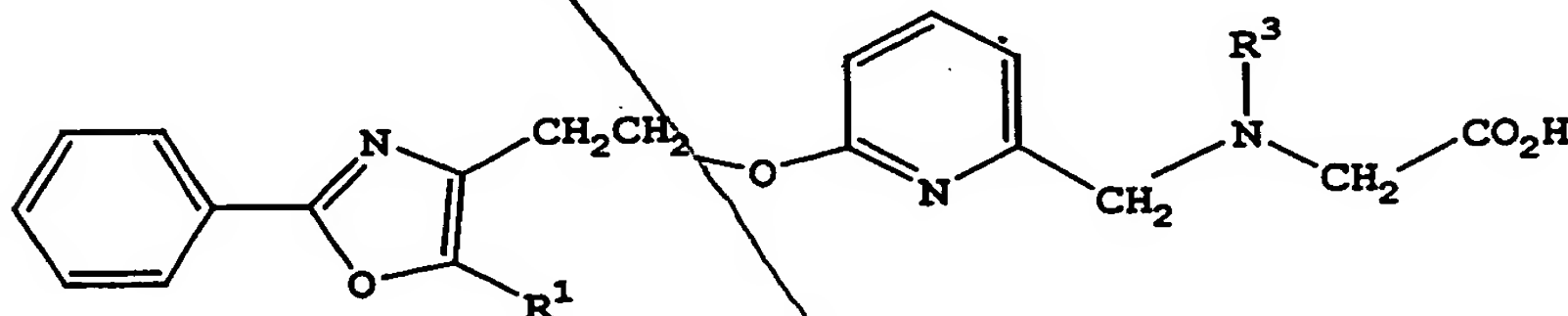
13. The compound as defined in Claim 1 wherein x is 2, m is 1, and n is 1.

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14. The compound as defined in Claim 1 having the structure

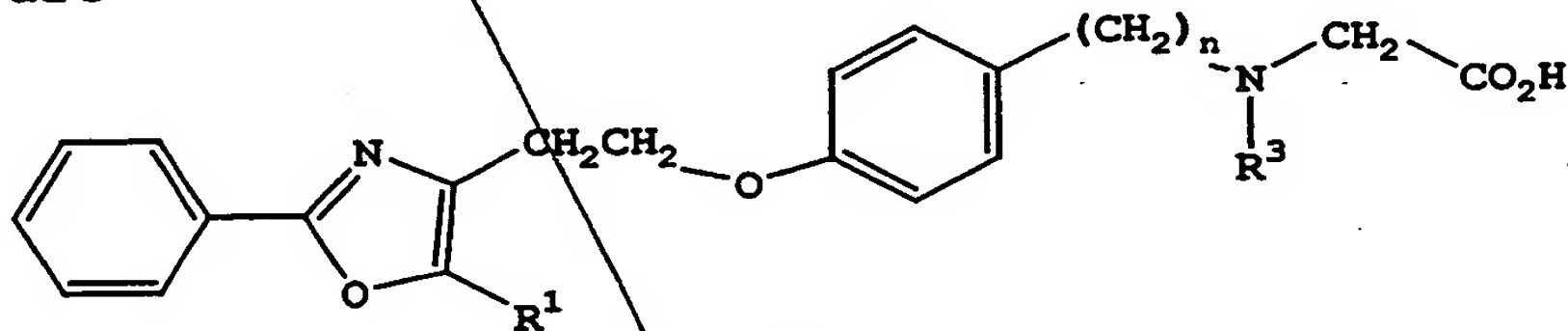


or

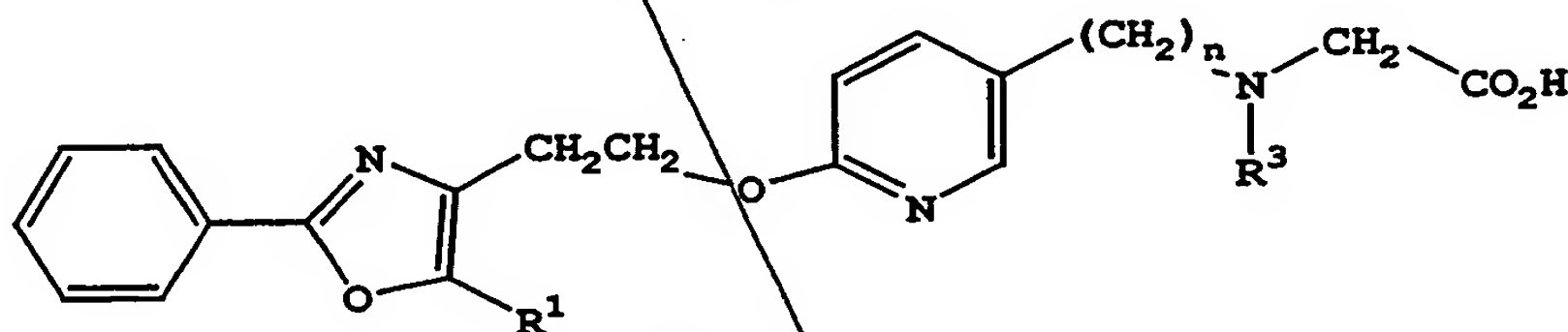


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15. The compound as defined in Claim 1 having the structure

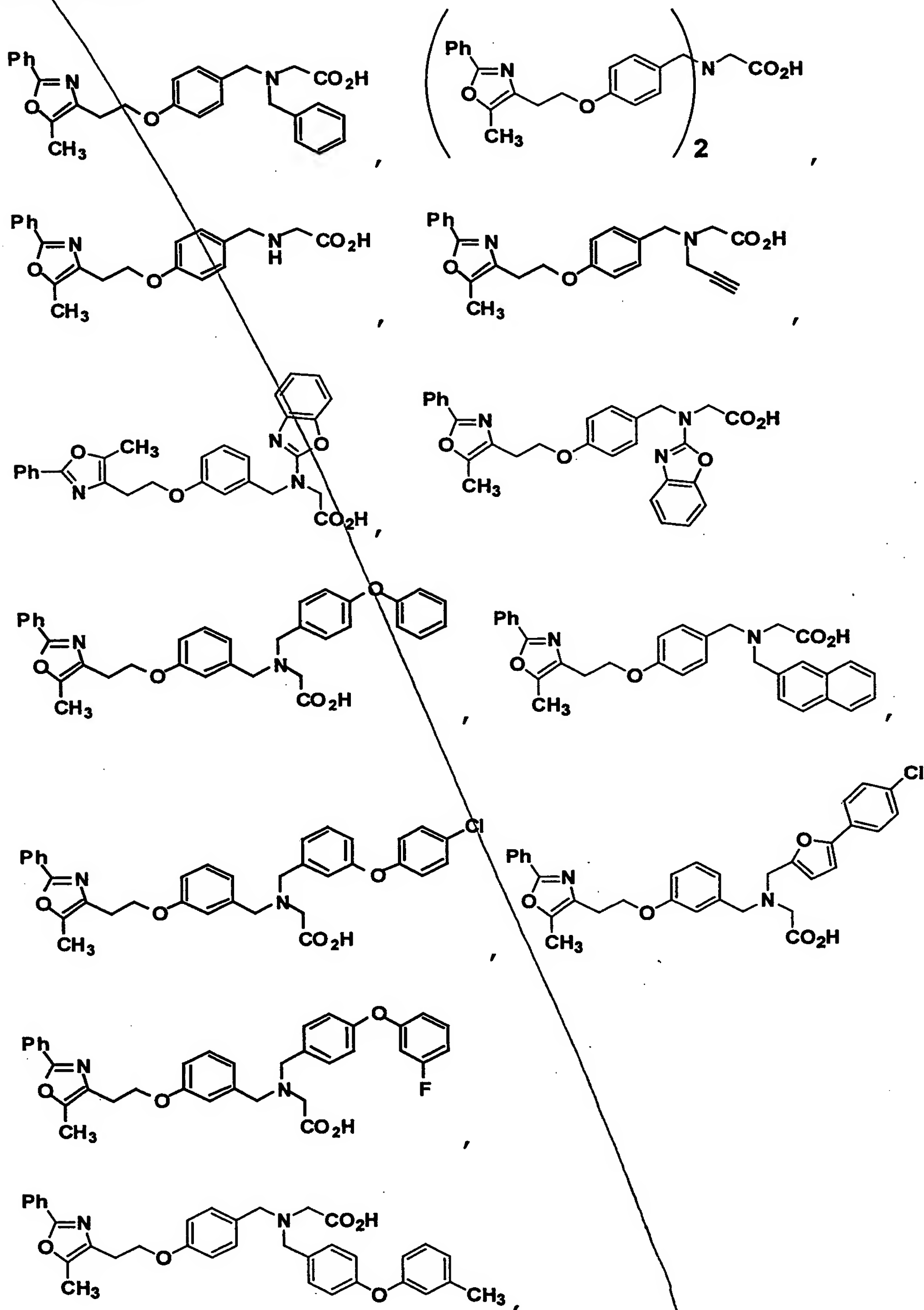


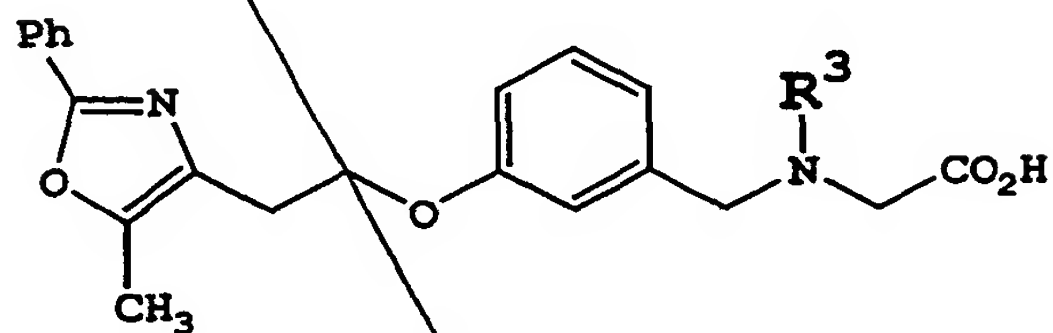
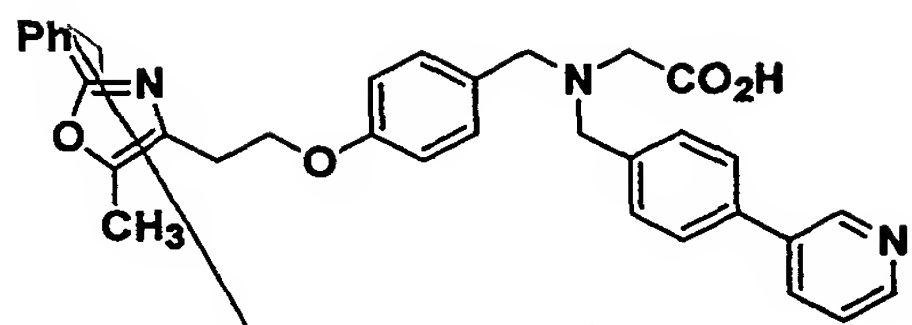
or



where $(CH_2)_n$ is CH_2 or $\begin{array}{c} CH_3 \\ | \\ -CH- \end{array}$.

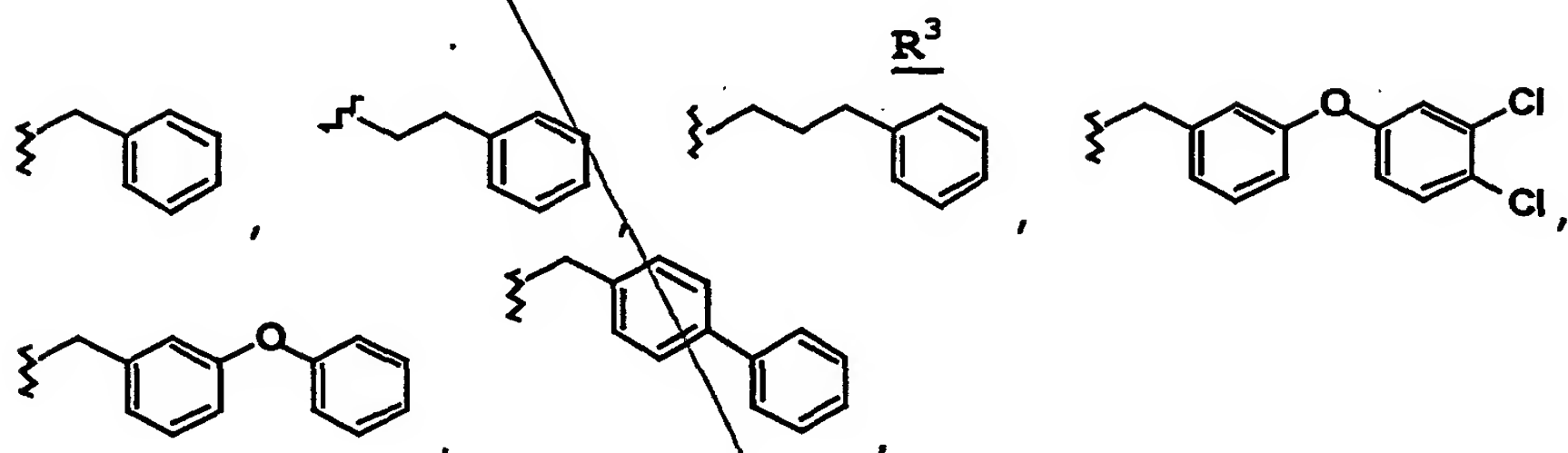
16. The compound as defined in Claim 1 having the structure



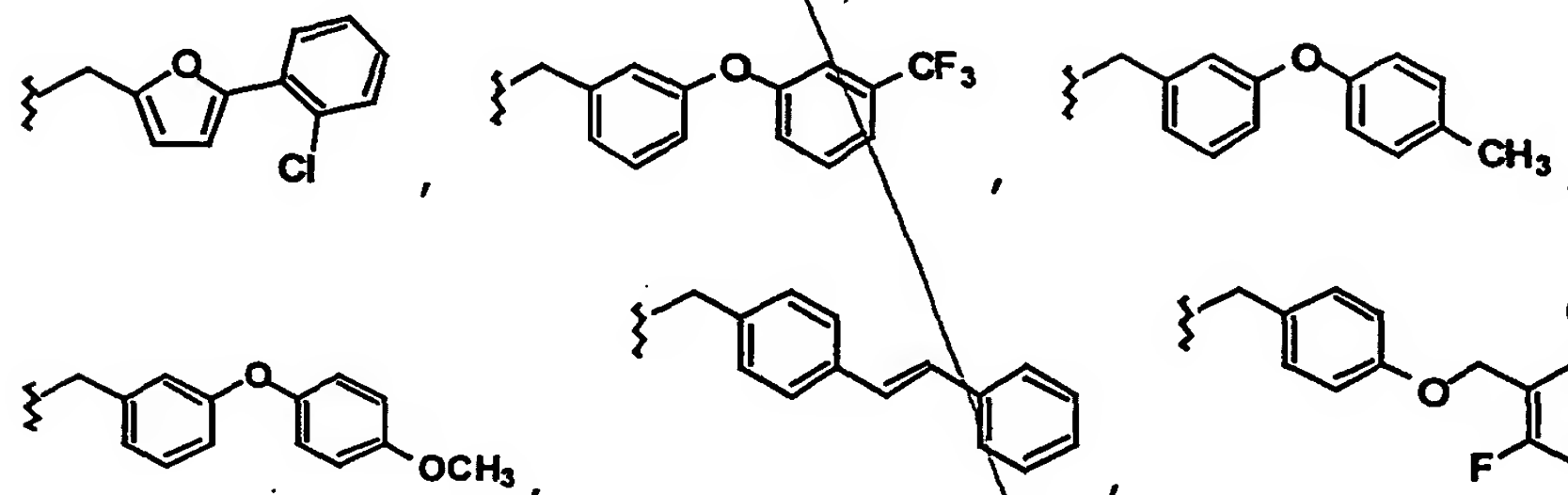


, where $R^3 =$

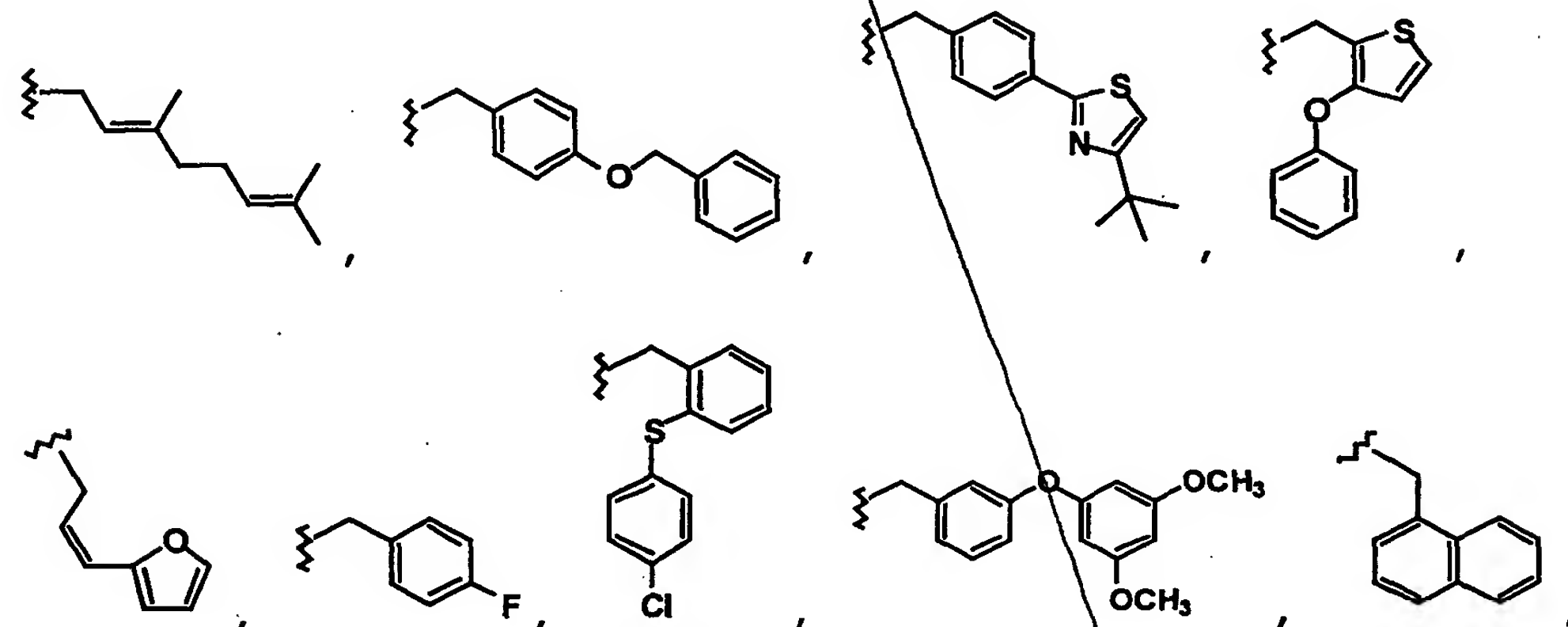
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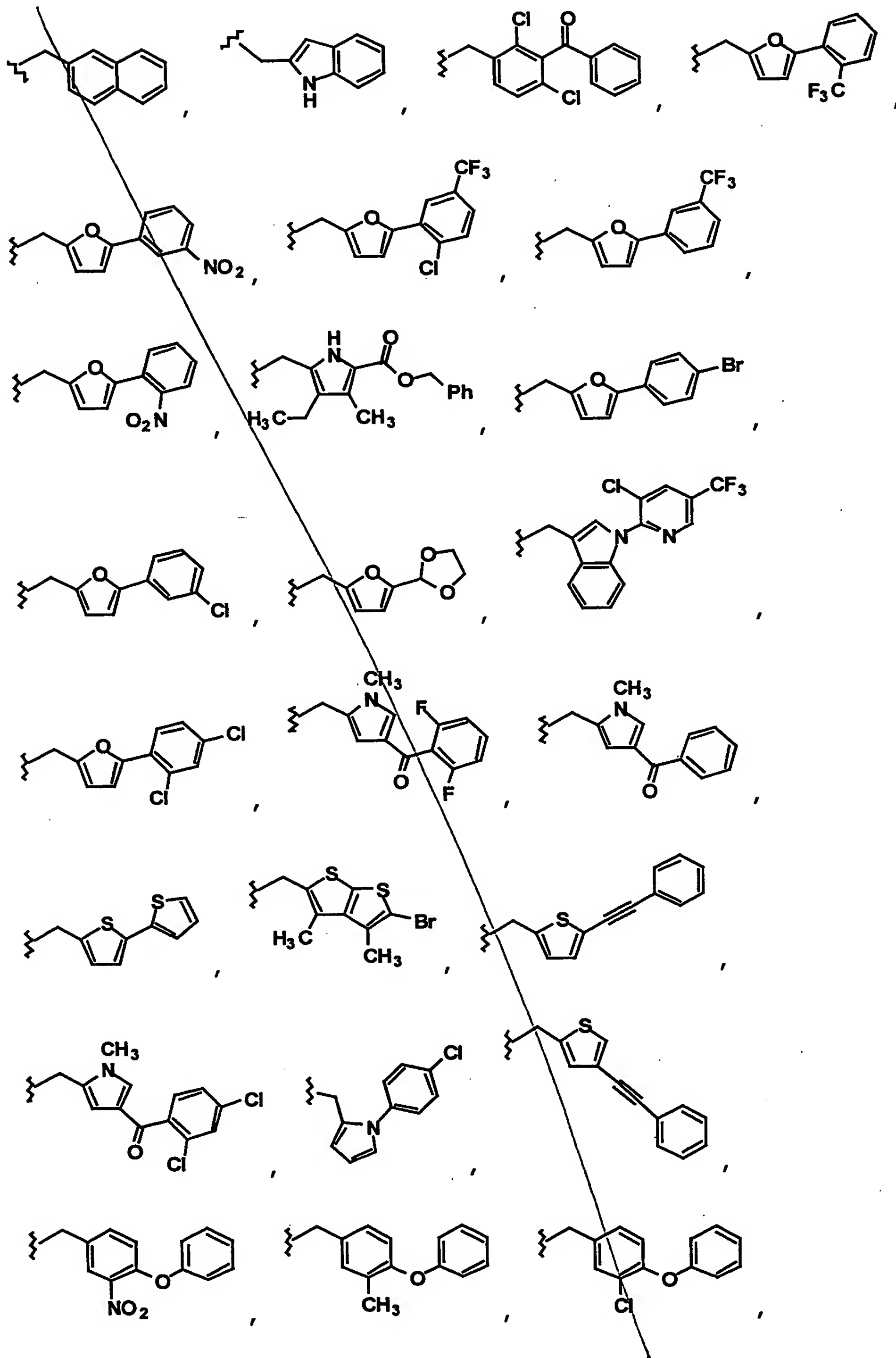


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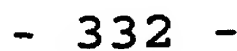
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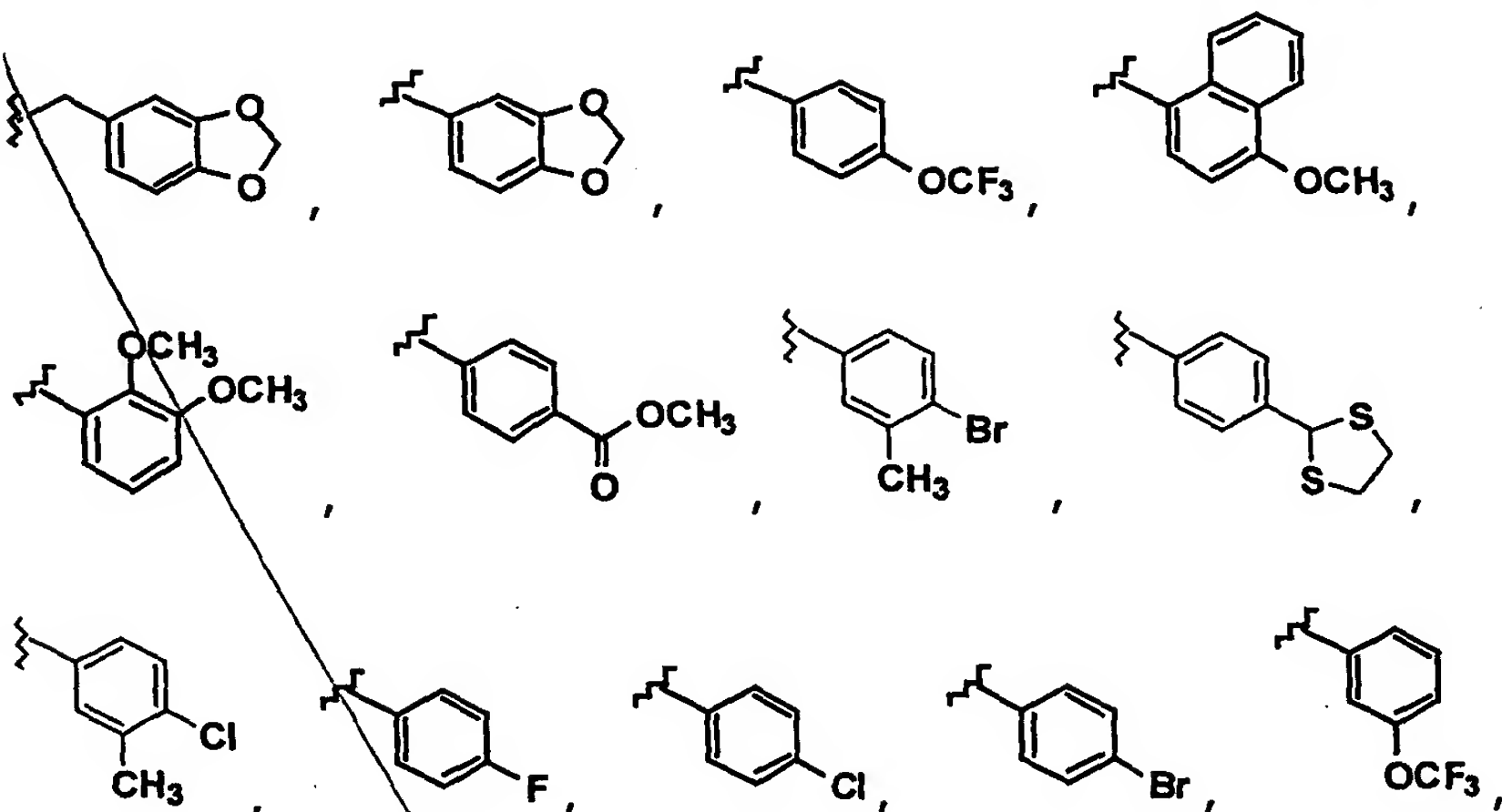
~~(S) -CH₃~~ ,
  ,
 (R) -CH₃ ,
  ,
  ,
 (R)

Cc1c(Cc2cc(OC)cc2)nc(C3=CC=CC=C3)o1CCOc4ccc(cc4)CN(Cc5ccc(cc5)C(=O)O)C(=O)Oc6cc(OC)cc6, Cc1c(Cc2cc(OC)cc2)nc(C3=CC=CC=C3)o1CCOc4ccc(cc4)CN(Cc5ccc(cc5)C(=O)O)C(=O)Oc6cc(Cl)cc(Cl)c6,
Cc1c(Cc2cc(OC)cc2)nc(C3=CC=CC=C3)o1CCOc4ccc(cc4)CN(Cc5ccc(cc5)C(=O)O)C(=O)Oc6ccc(OC)c6, Cc1c(Cc2cc(OC)cc2)nc(C3=CC=CC=C3)o1CCOc4ccc(cc4)CN(Cc5ccc(cc5)C(=O)O)C(=O)Oc6ccc(OCF2)c6,
Cc1c(Cc2cc(OC)cc2)nc(C3=CC=CC=C3)o1CCOc4ccc(cc4)CN(Cc5ccc(cc5)C(=O)O)C(=O)Oc6ccc(OCF2)c6, Cc1c(Cc2cc(OC)cc2)nc(C3=CC=CC=C3)o1CCOc4ccc(cc4)CN(Cc5ccc(cc5)C(=O)O)C(=O)Oc6ccc(O)cc6

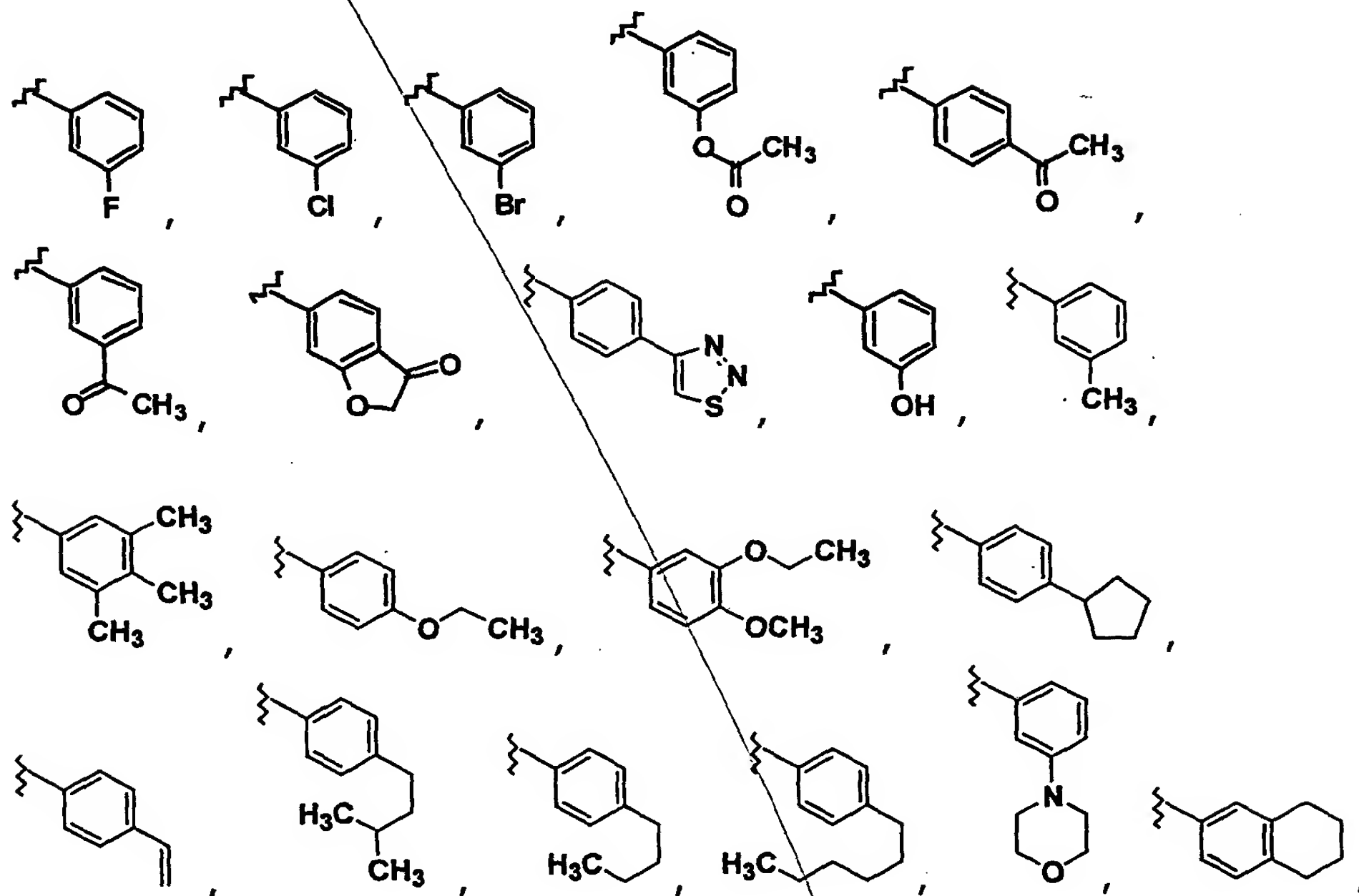


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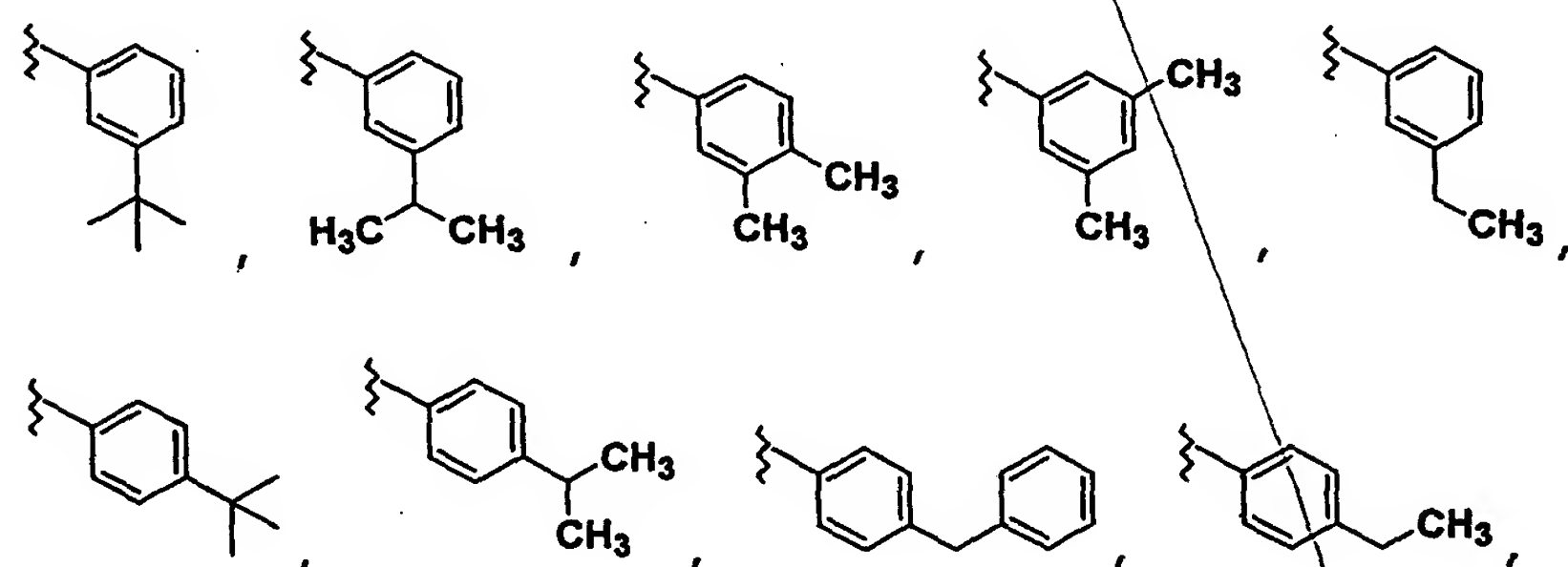
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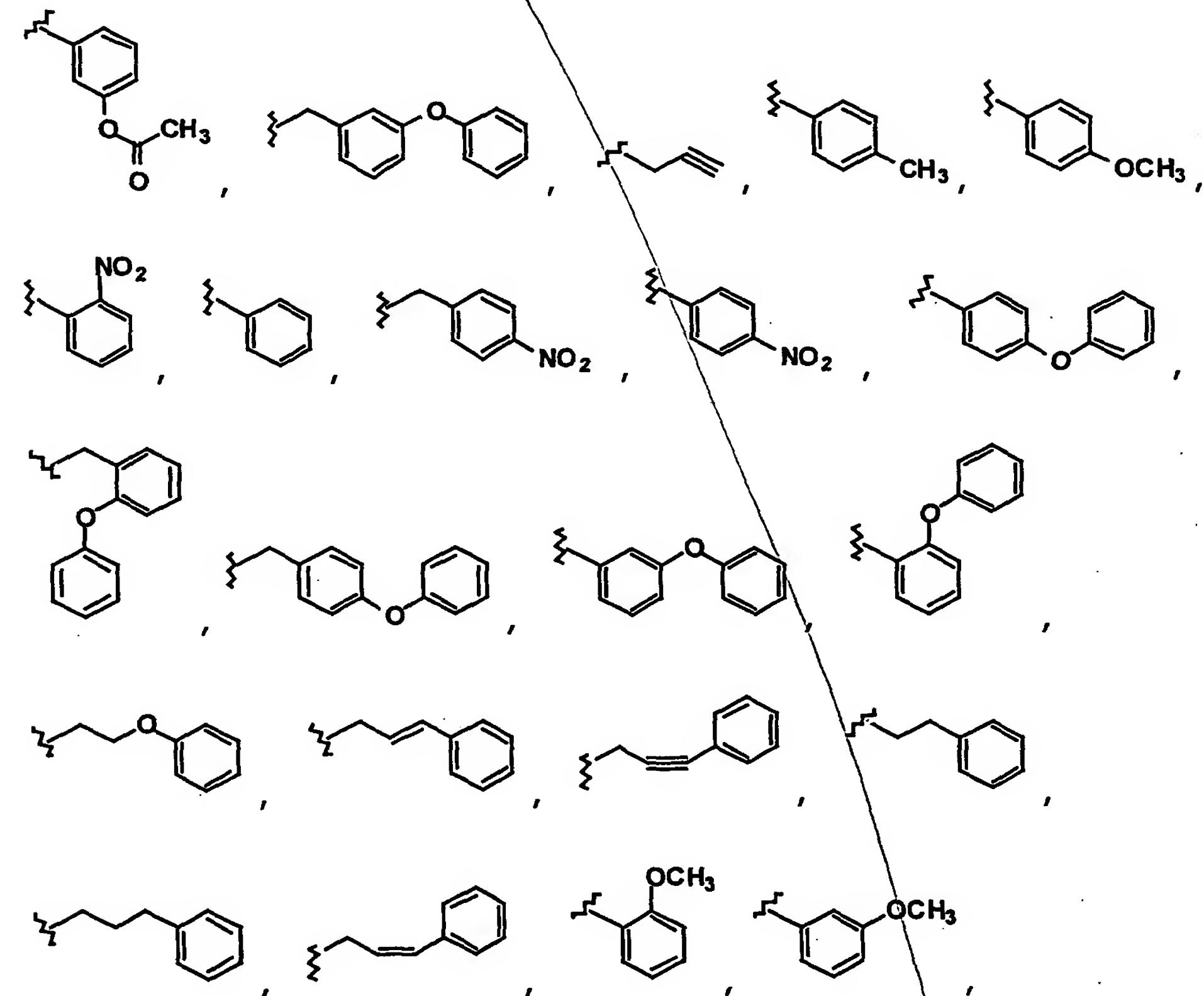
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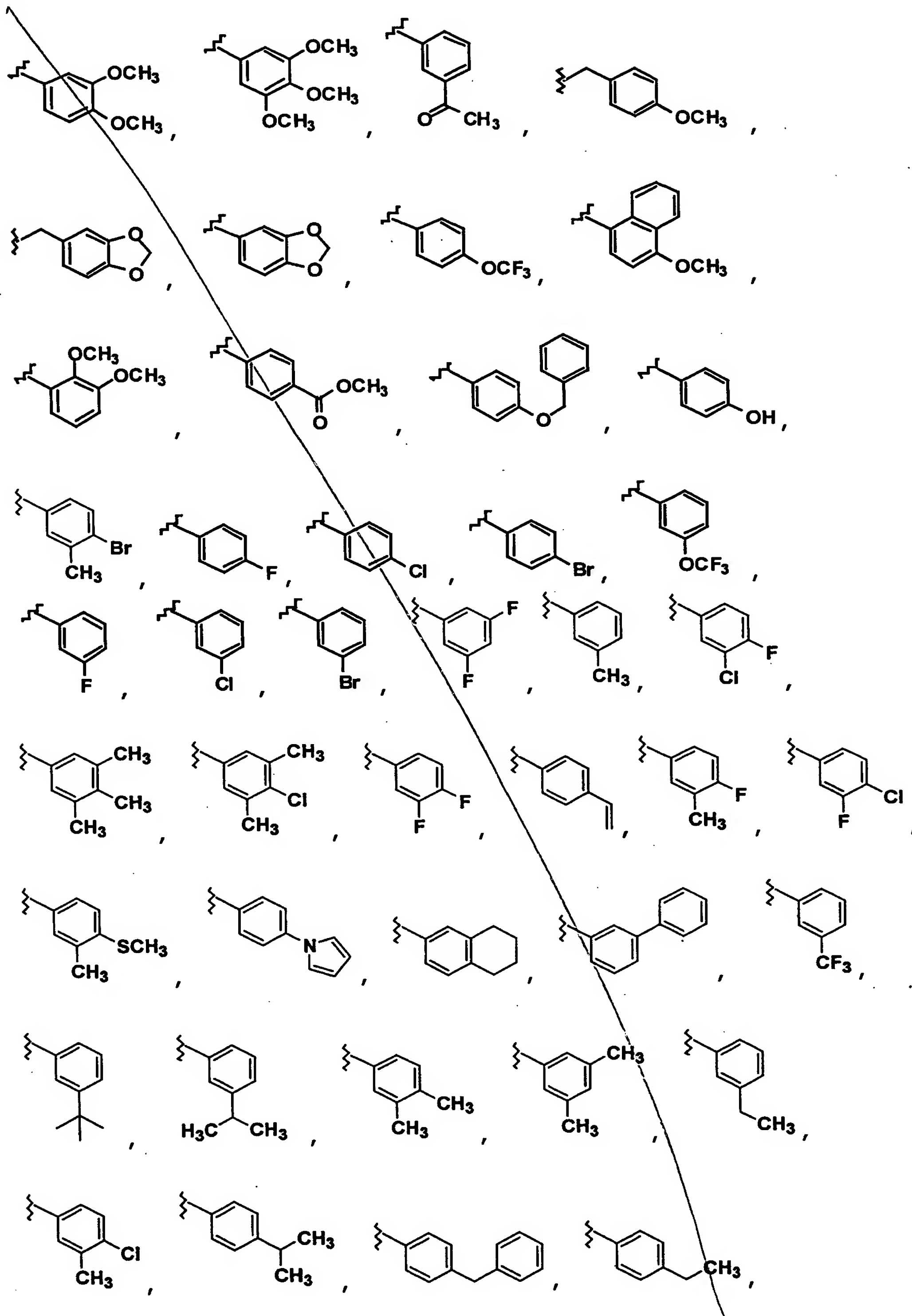
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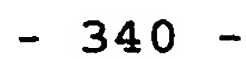
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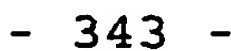


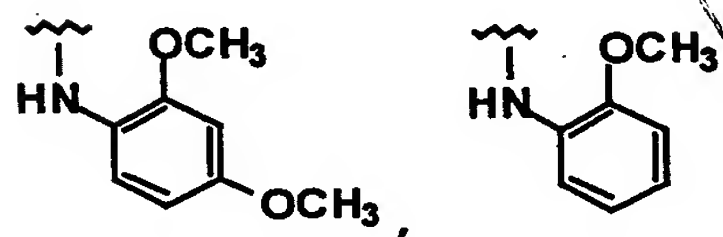
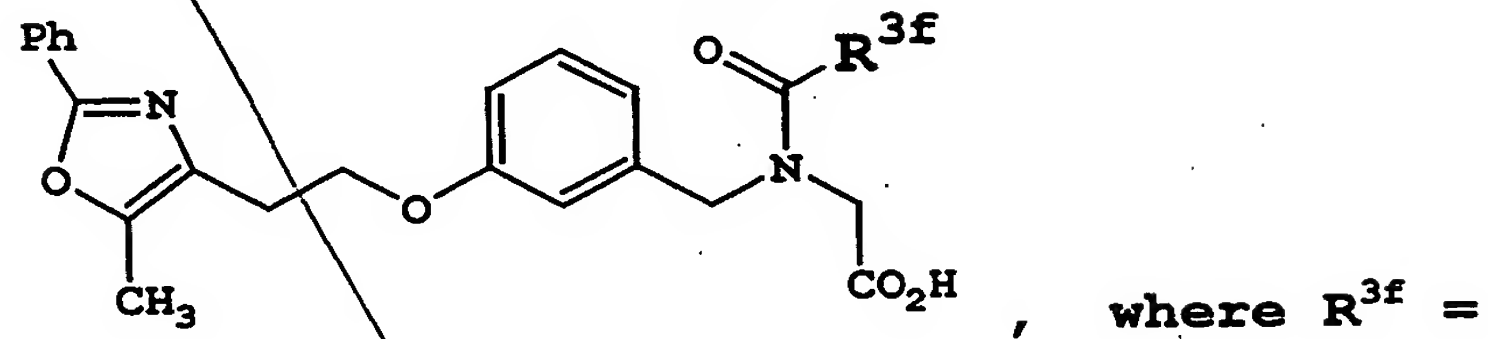
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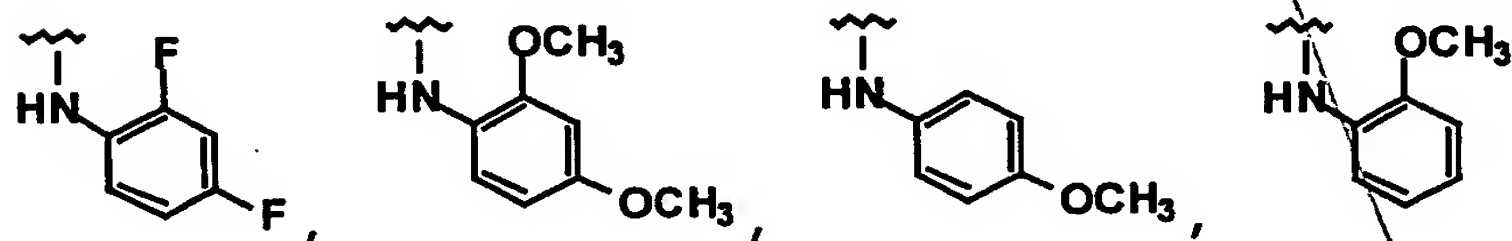
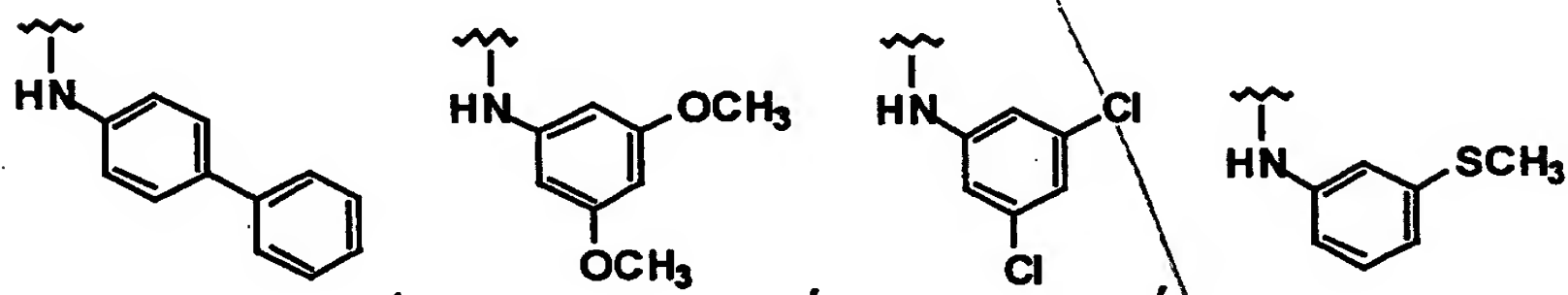
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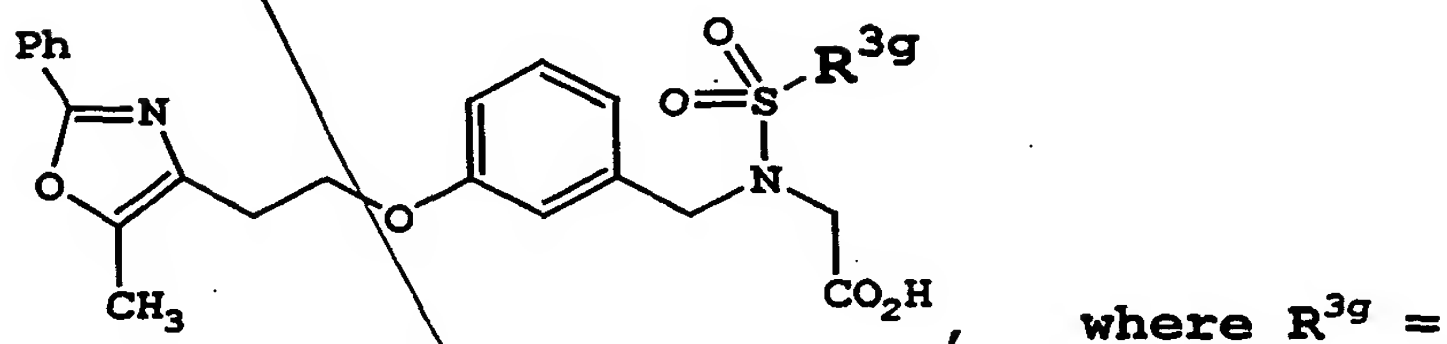
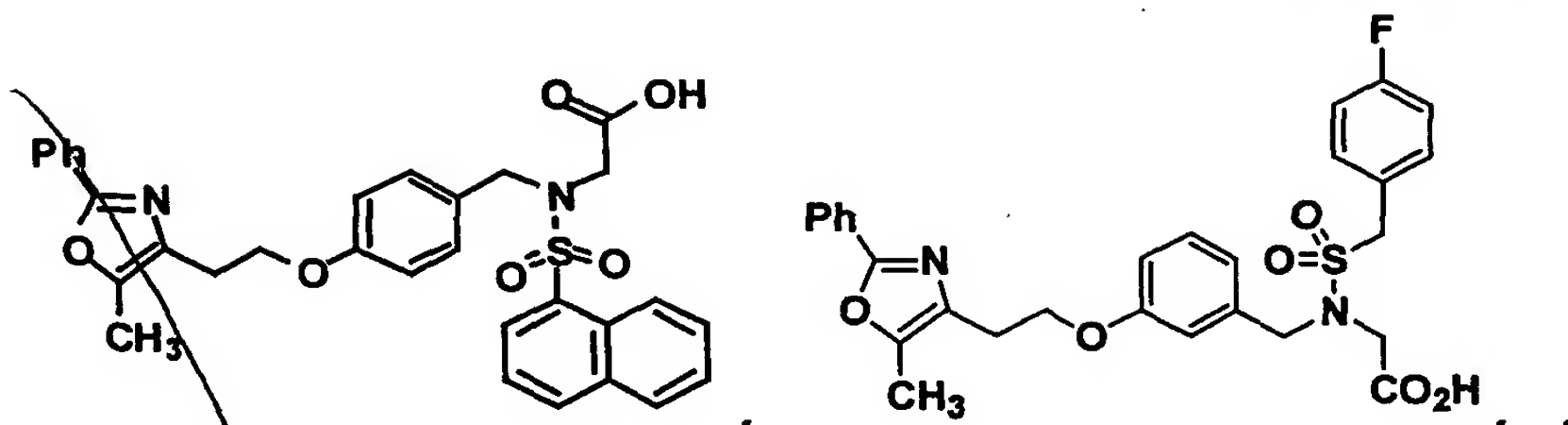




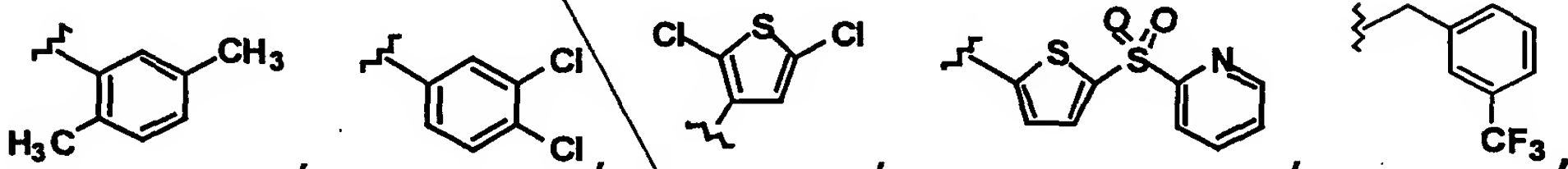
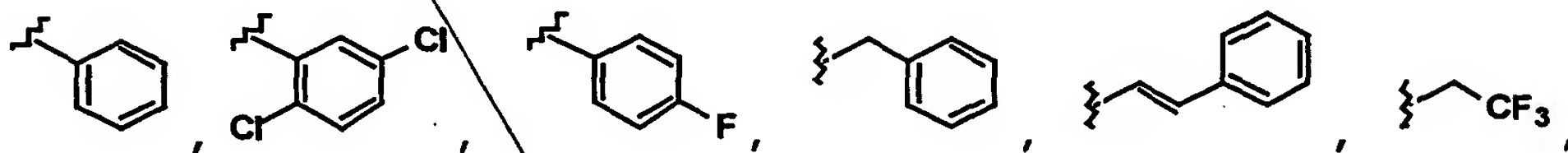


, where $R^{3f} =$

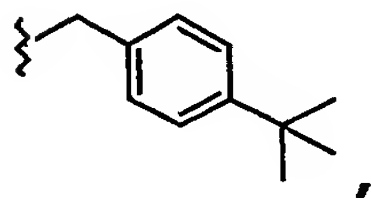
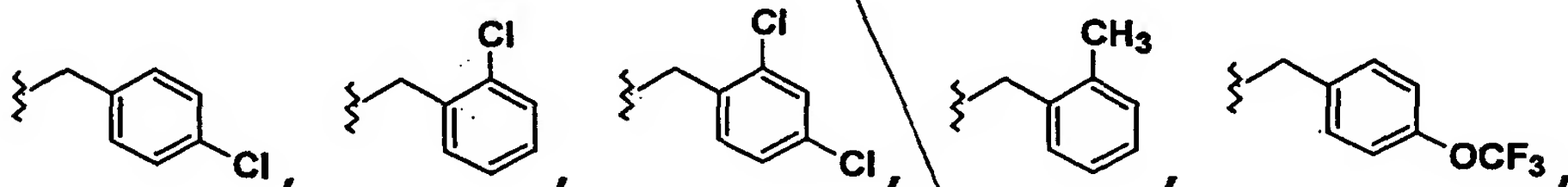
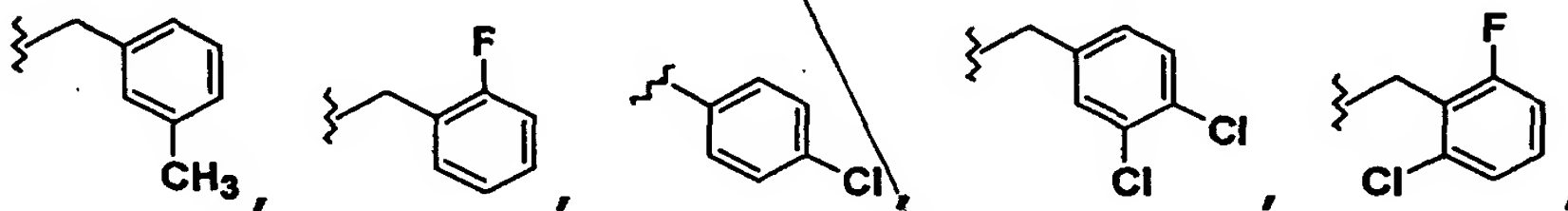




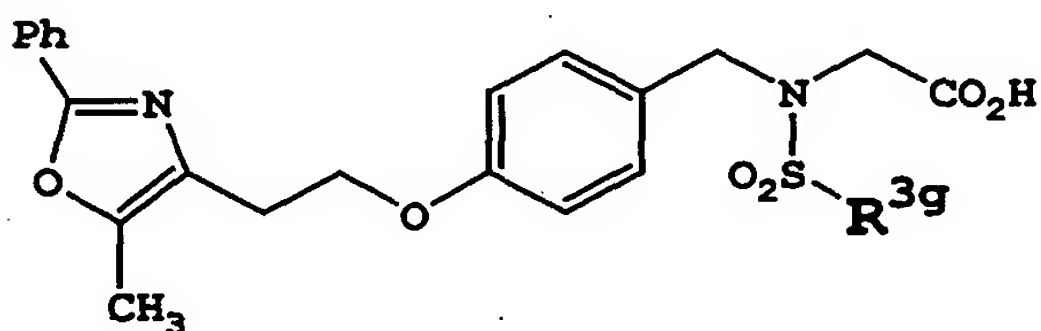
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where R^{3g} =

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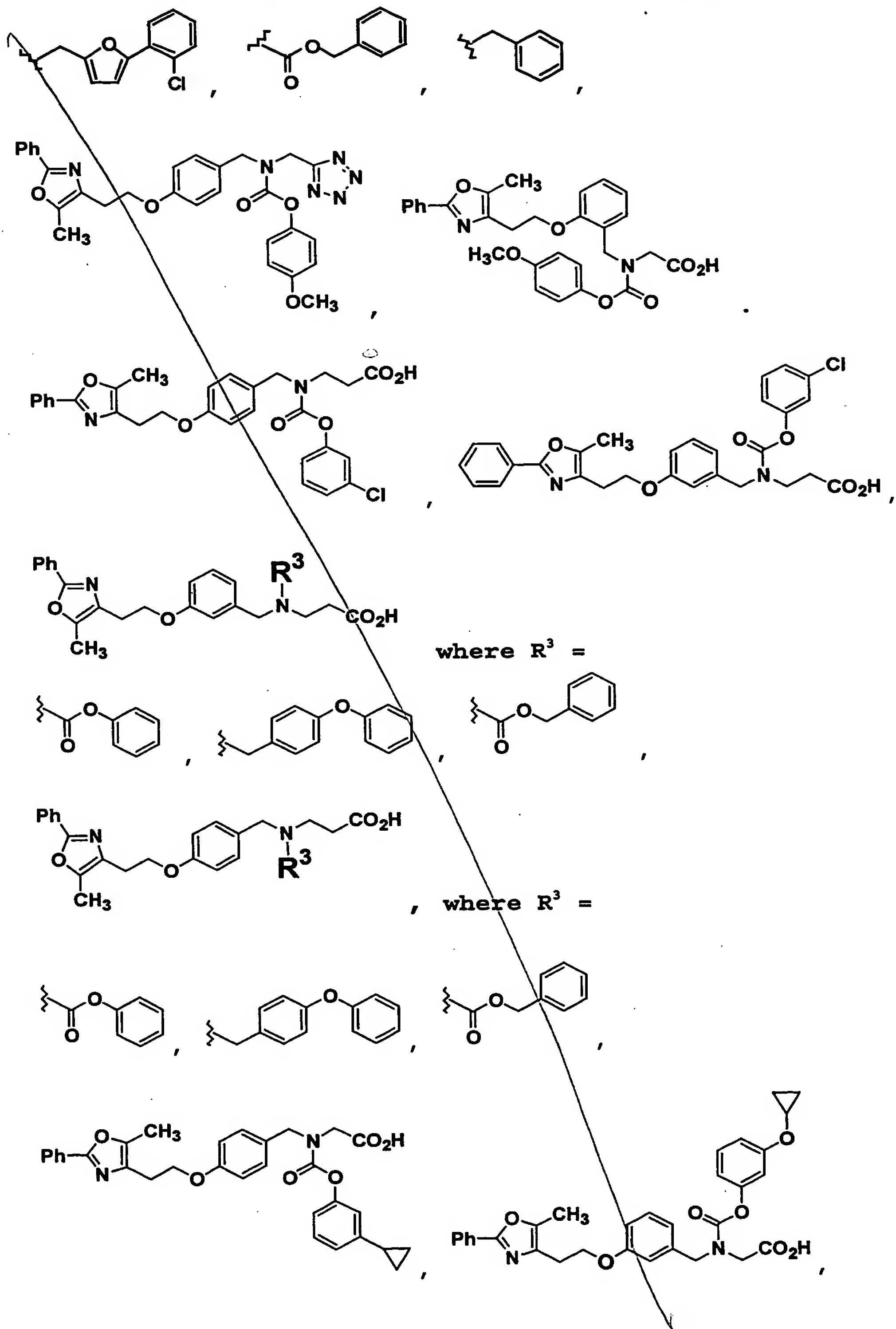
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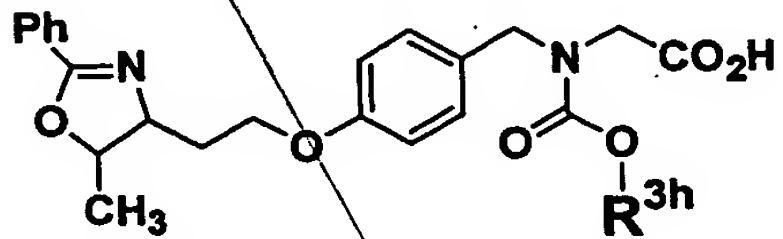


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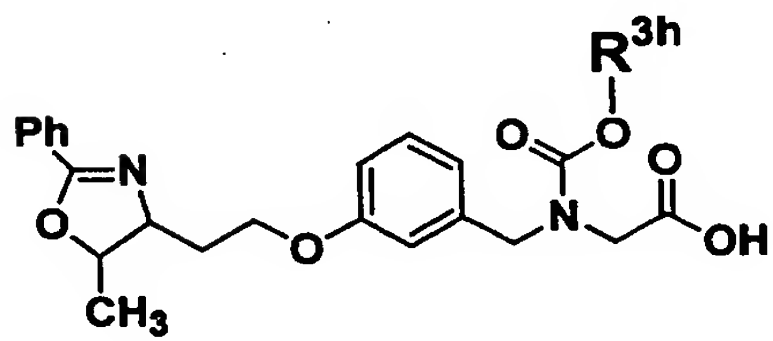
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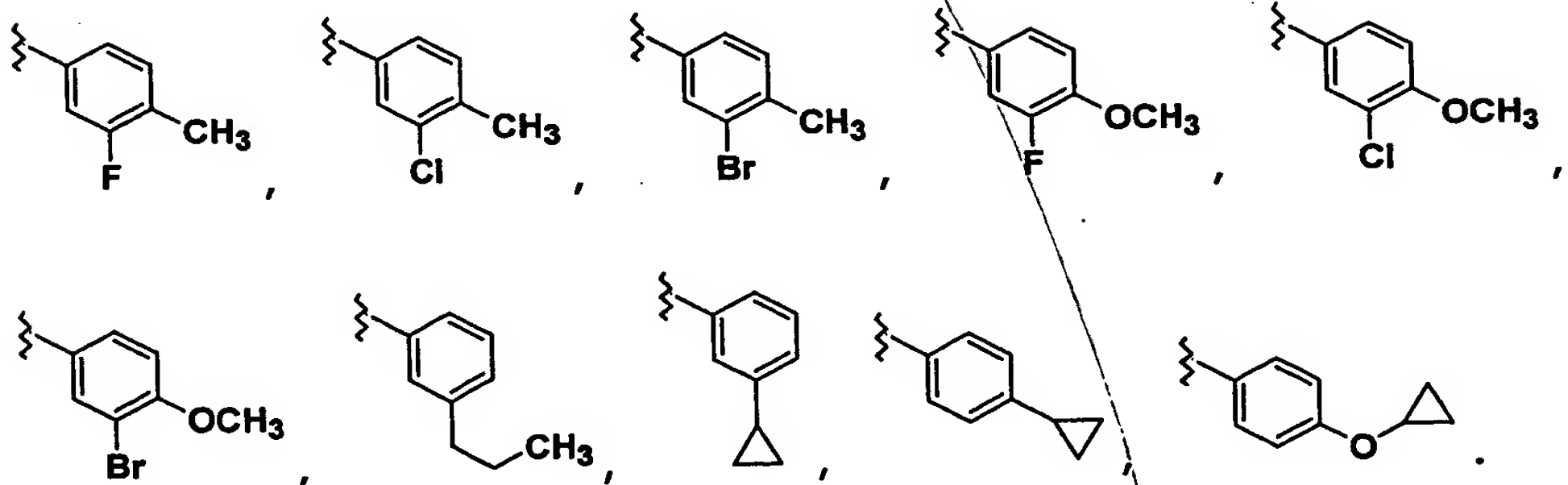




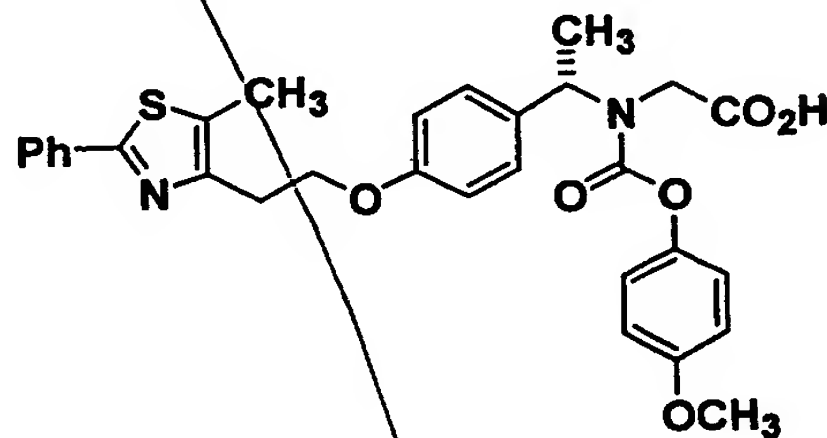
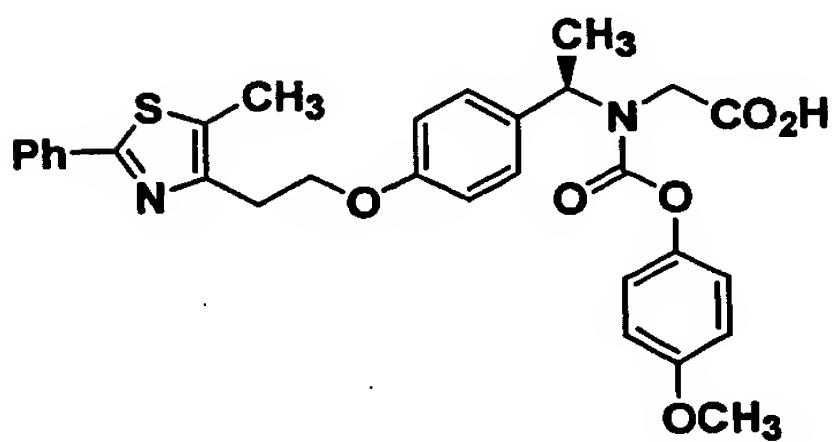
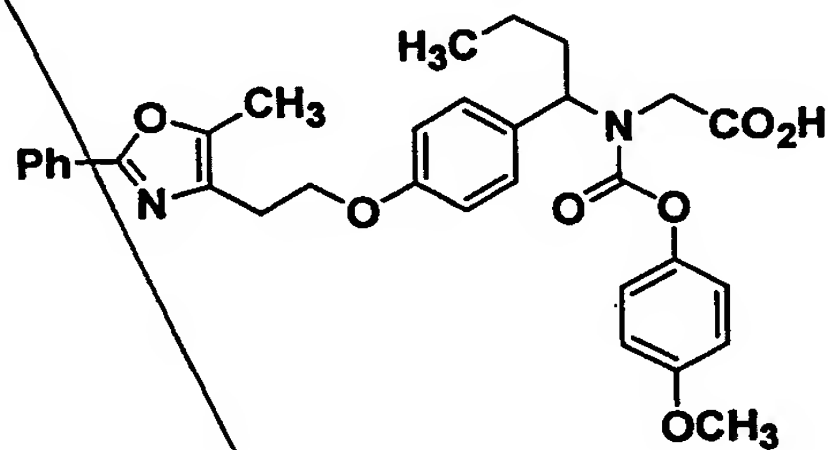
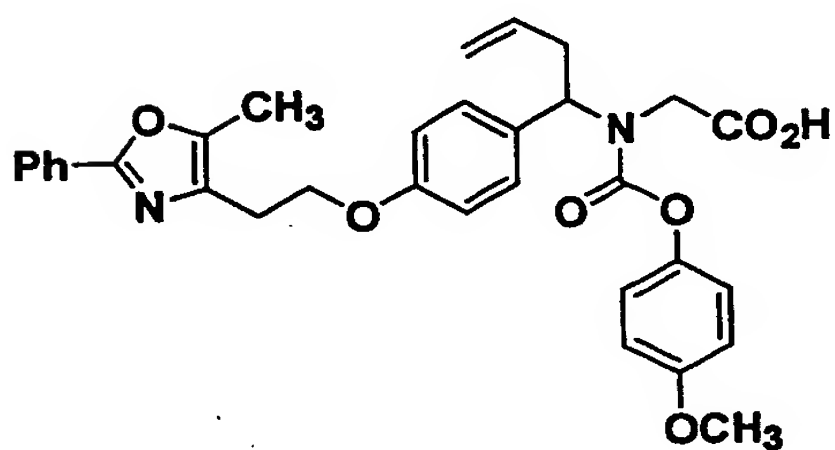
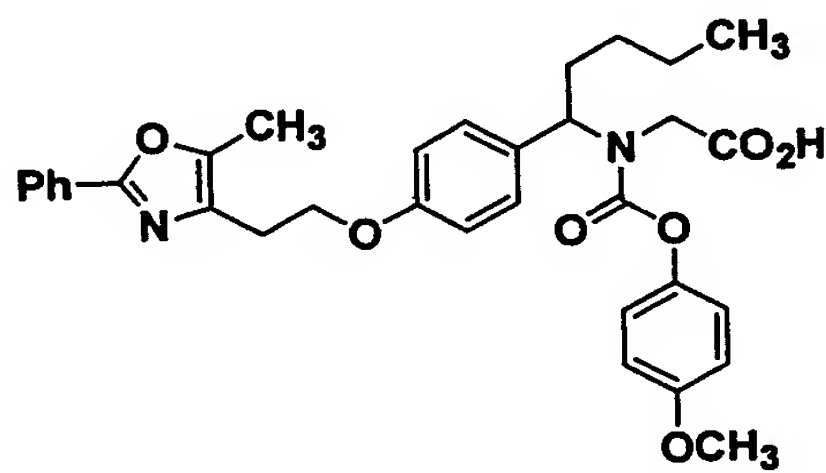
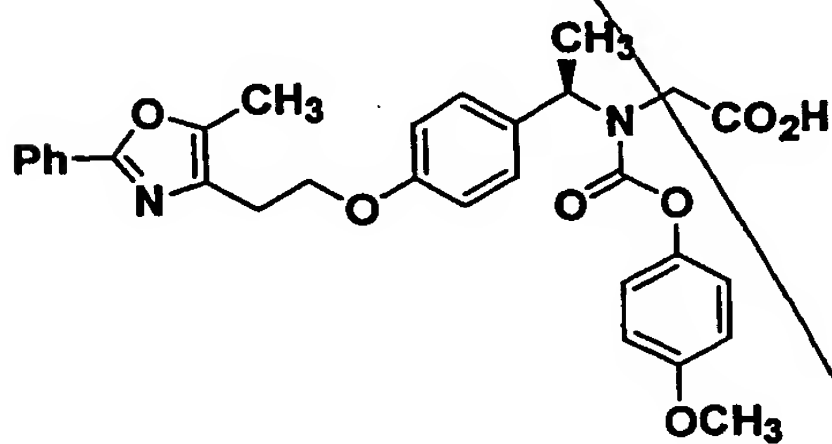
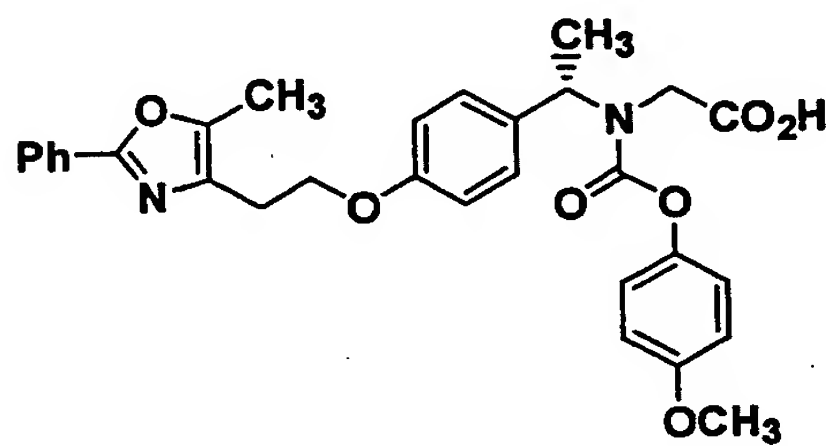
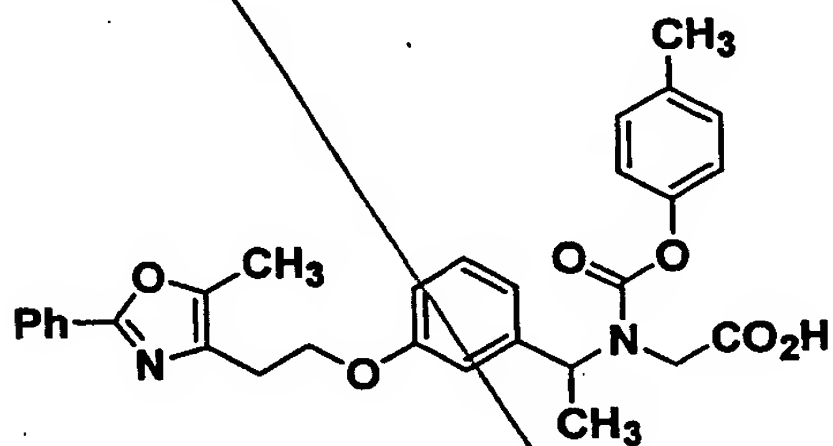
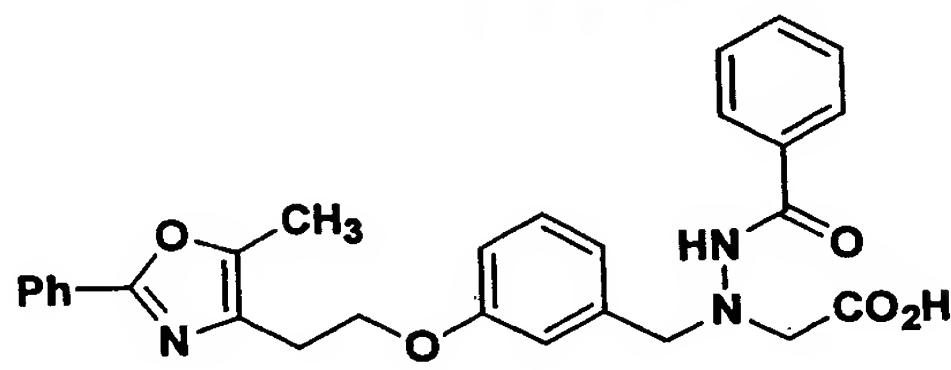
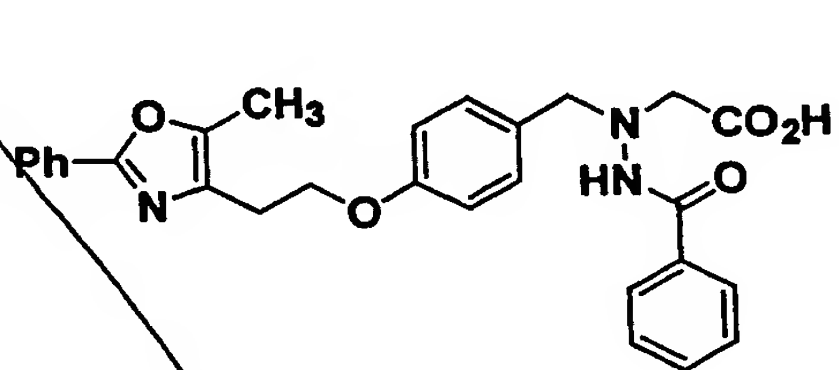
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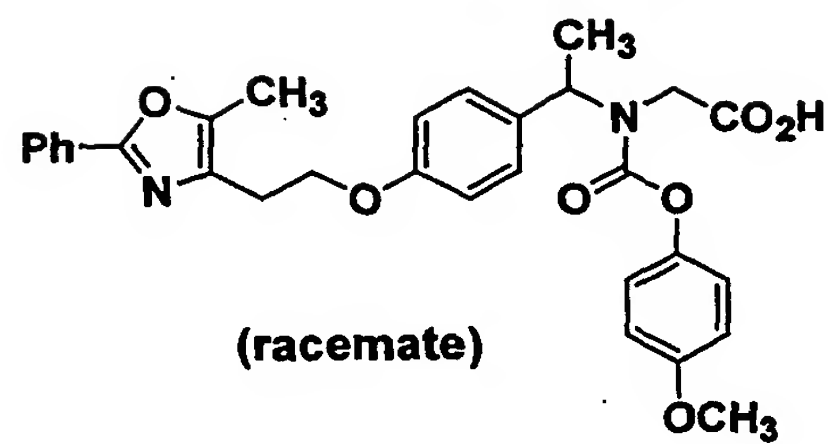
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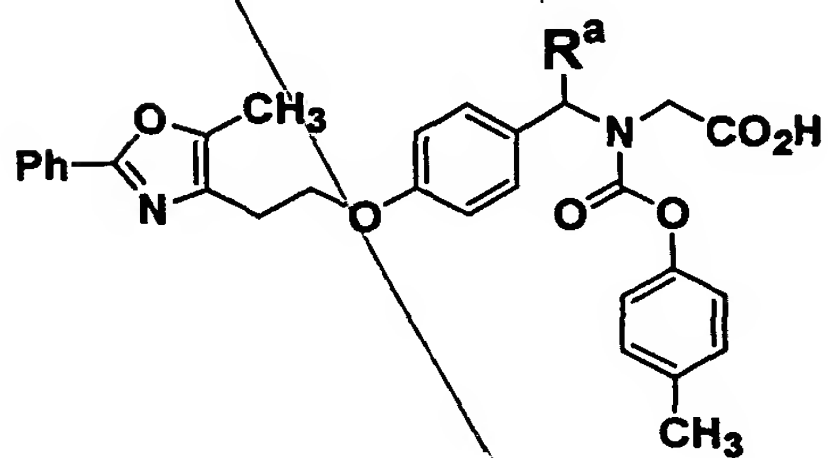
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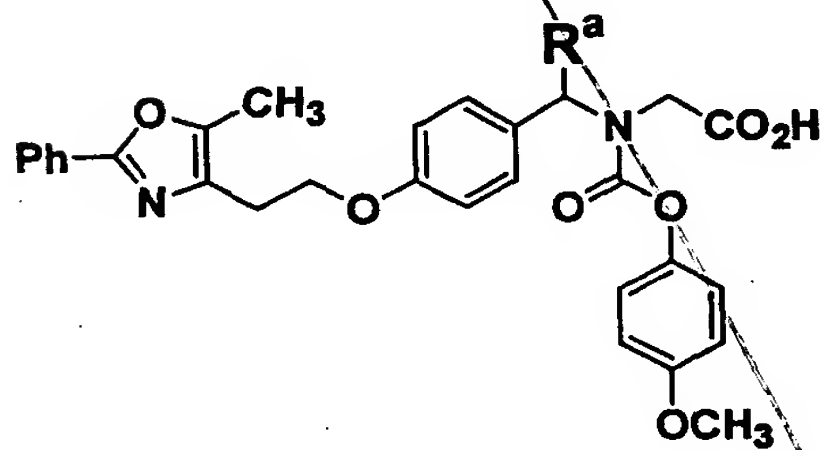
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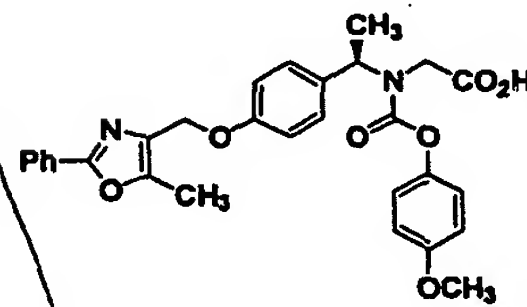
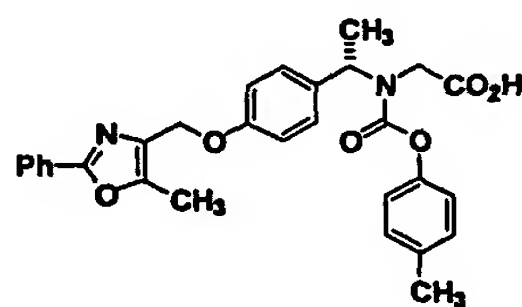
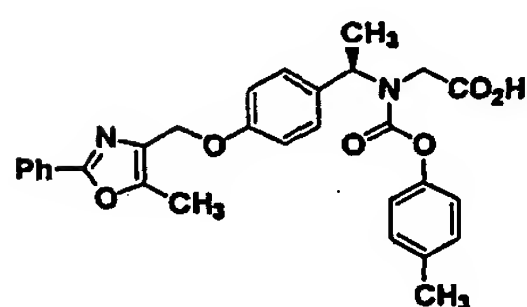
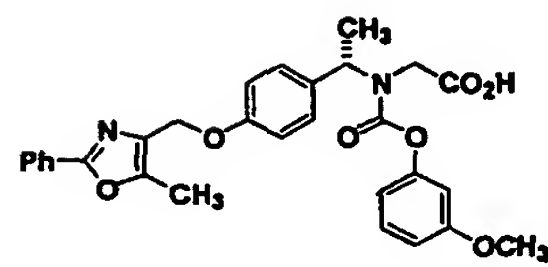
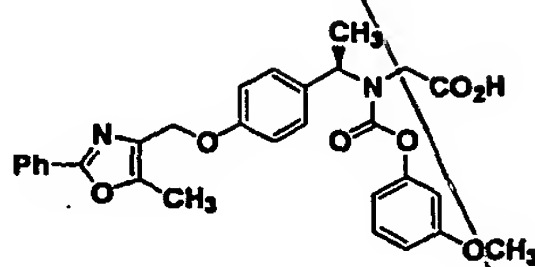
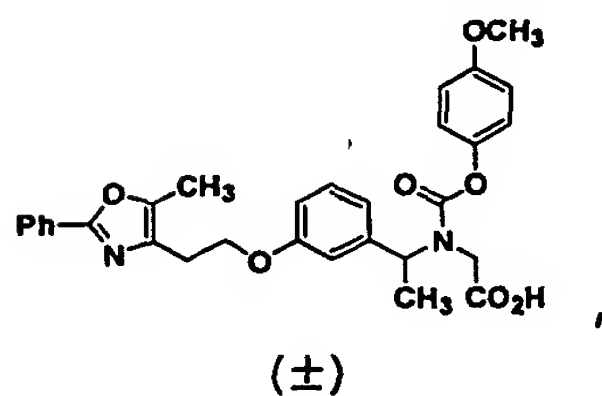
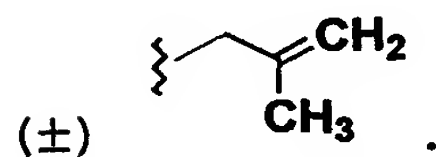
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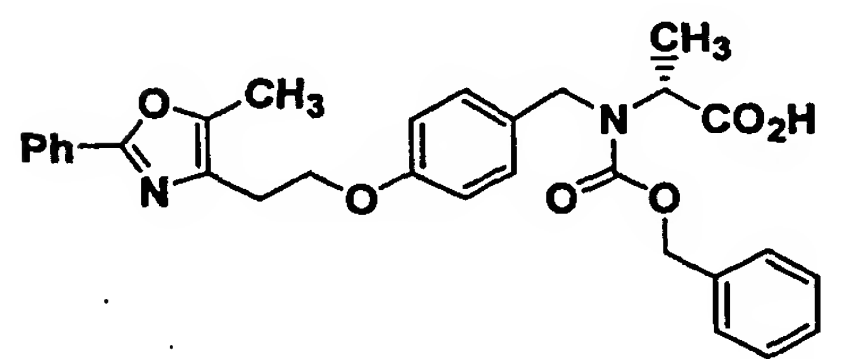
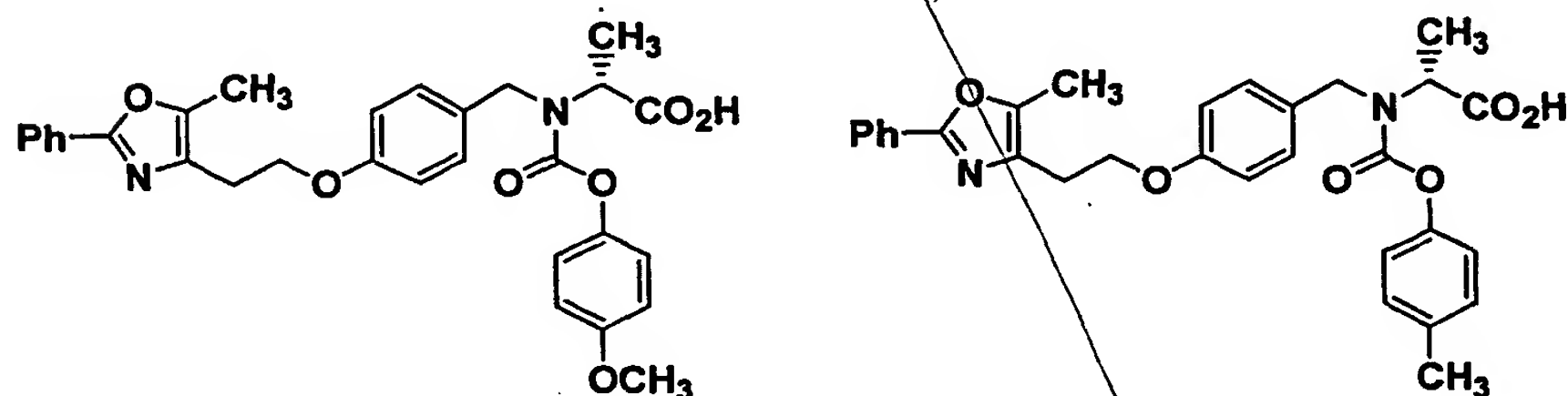
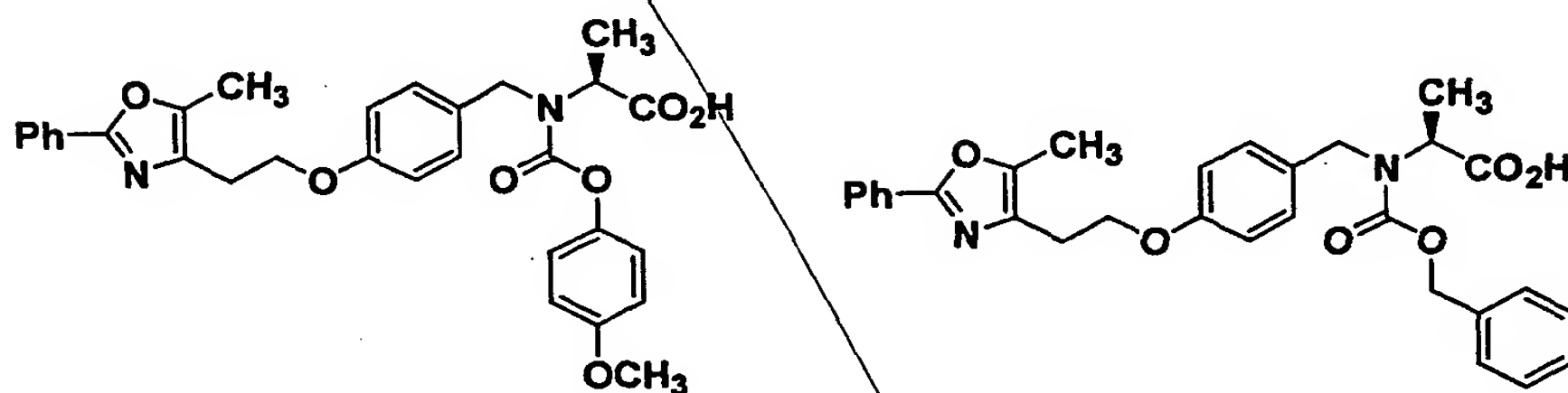
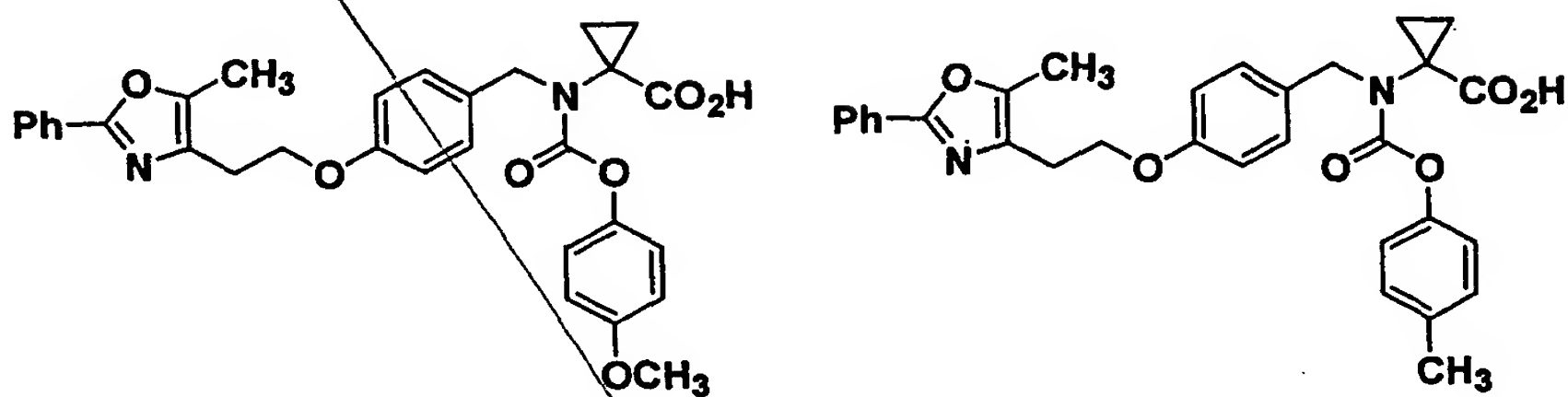
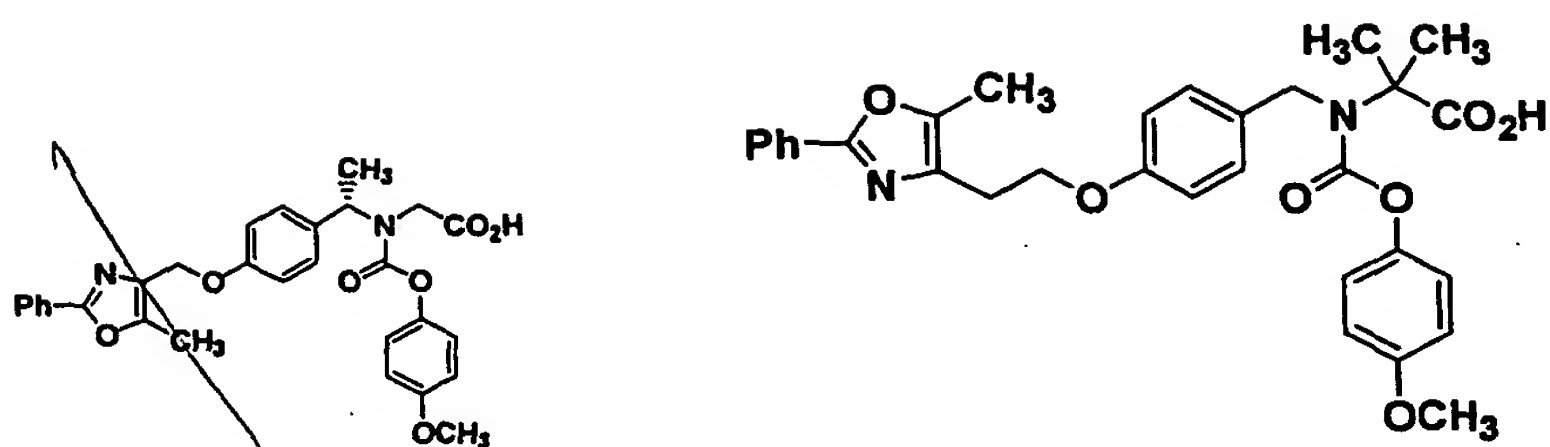


where $R^a = (\pm)\text{-Me}$, $(\pm)\text{ n-Bu}$,



where $R^a = (\pm) Et, (\pm) i-Bu,$



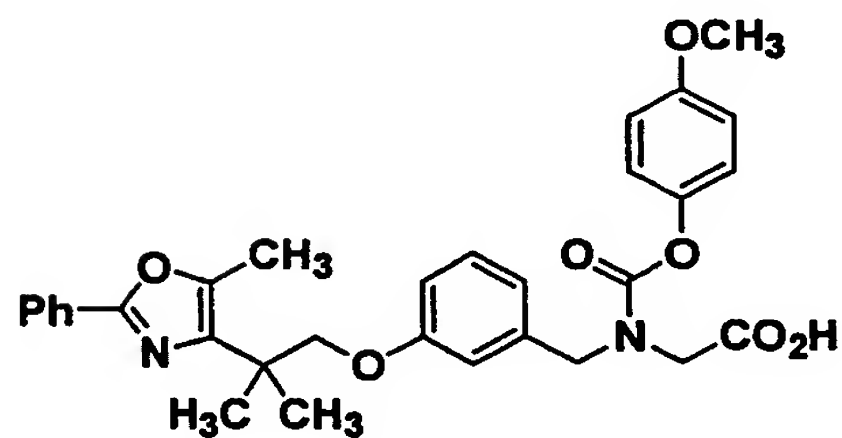
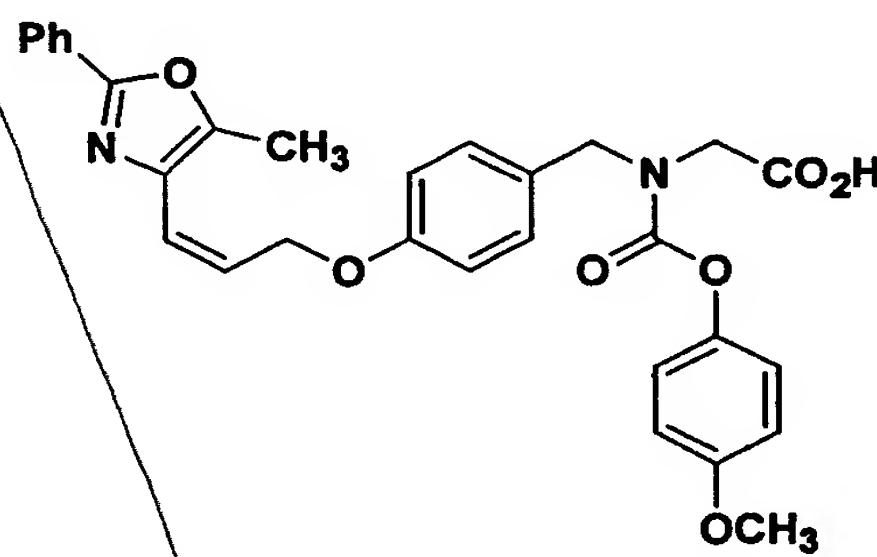
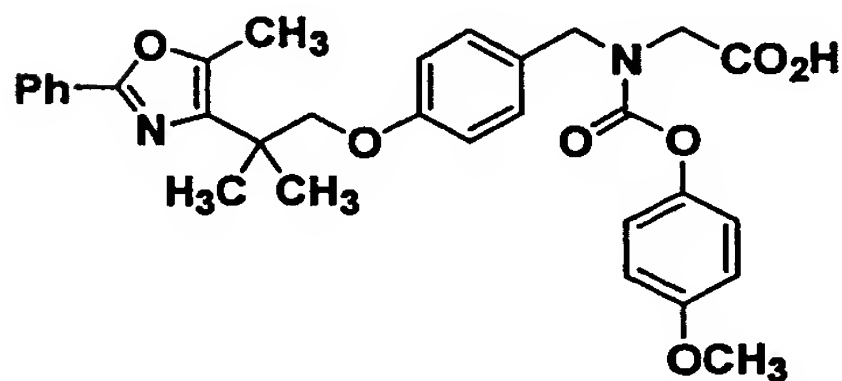
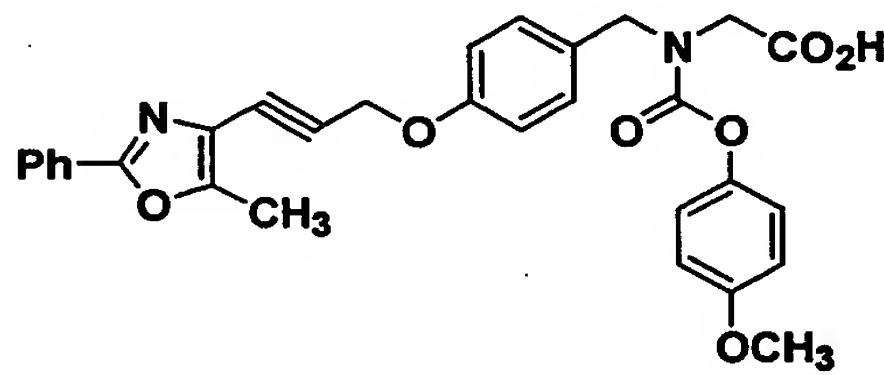
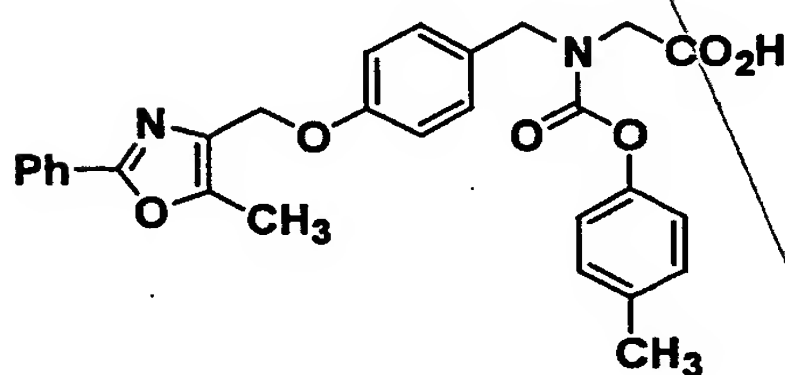
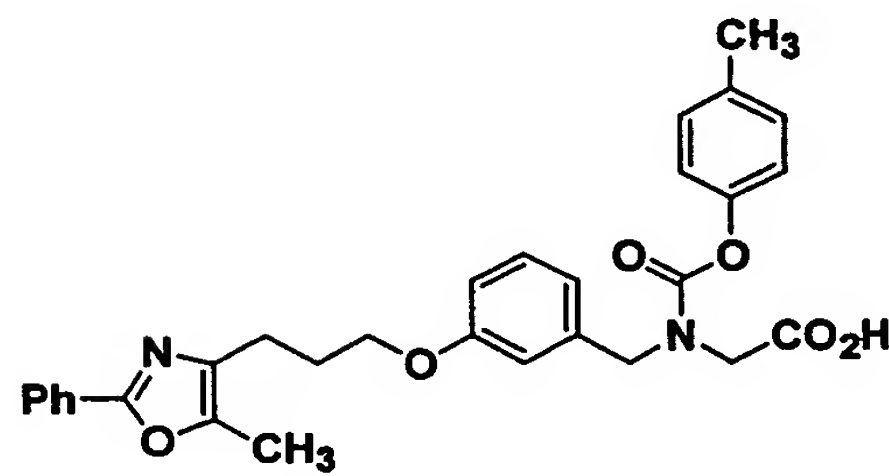
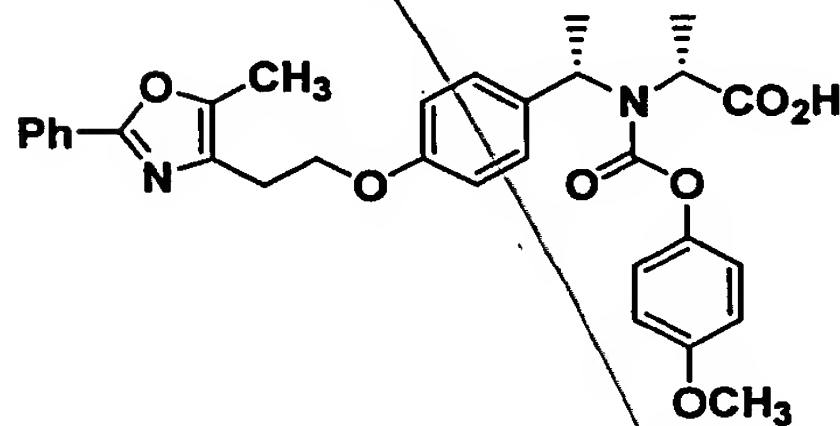
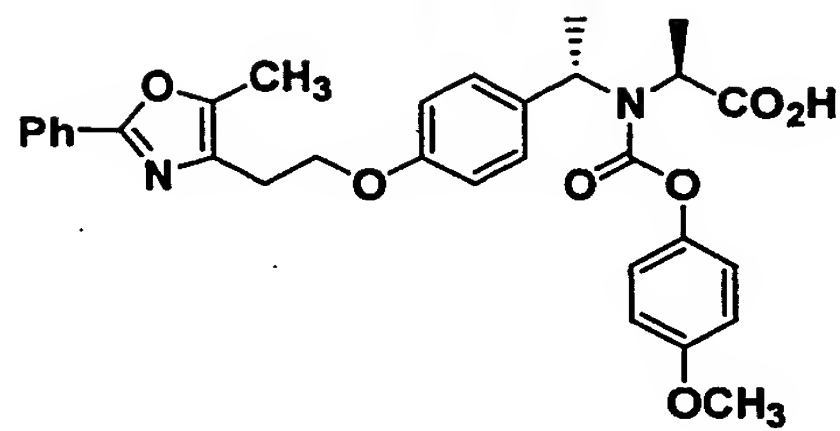
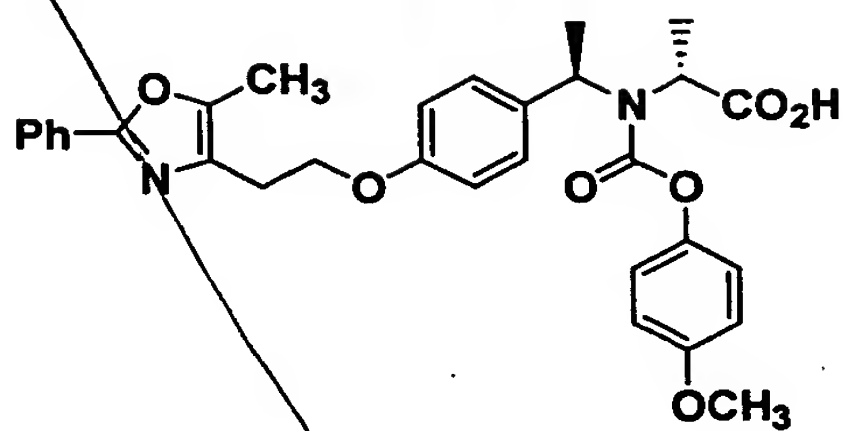


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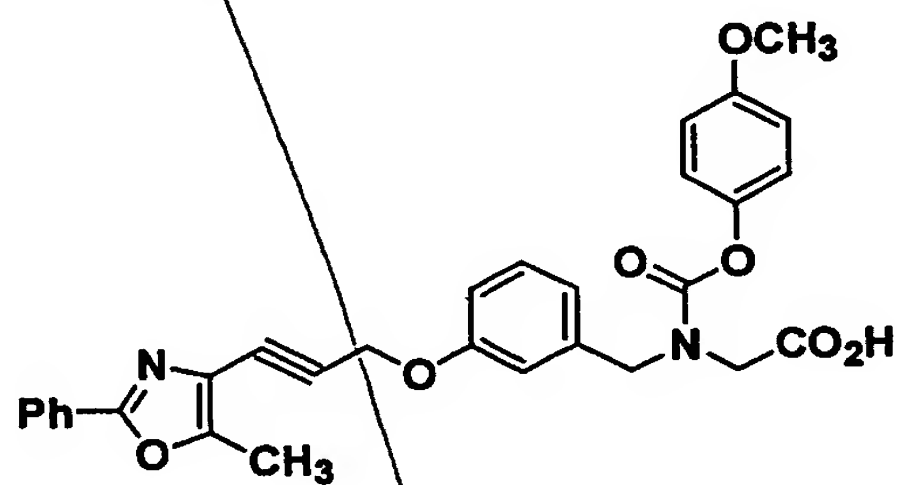
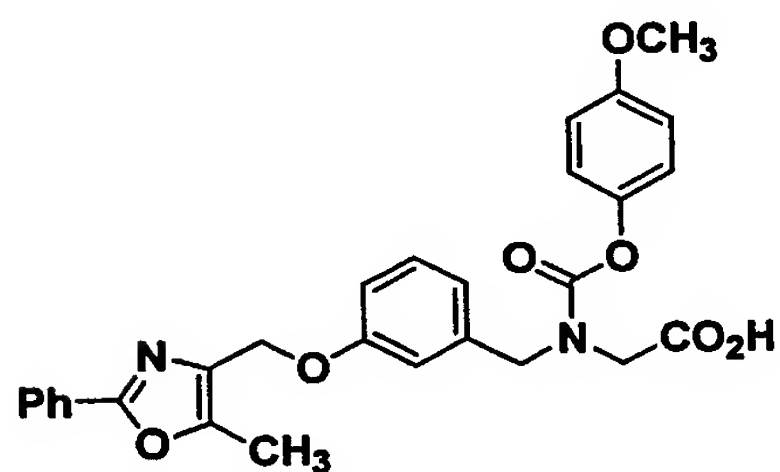
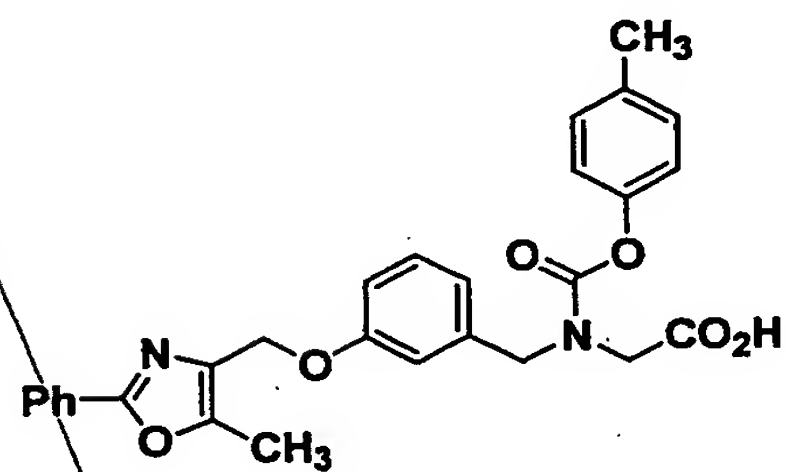
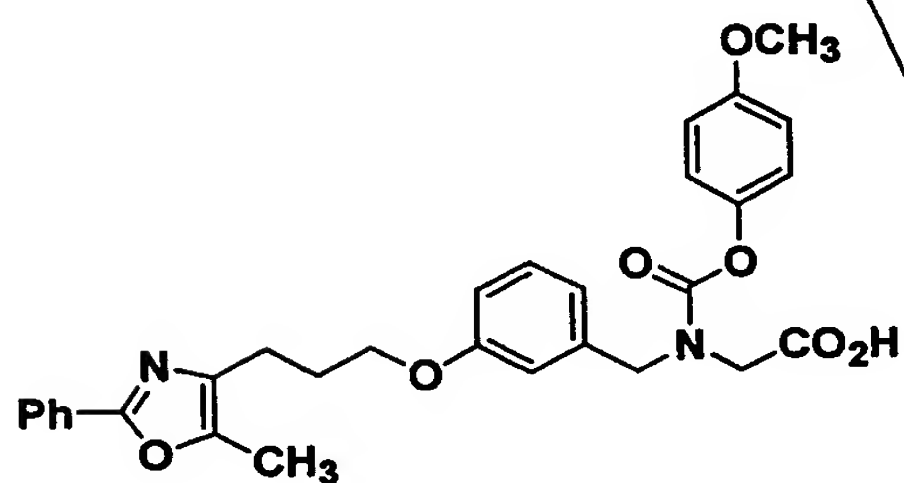
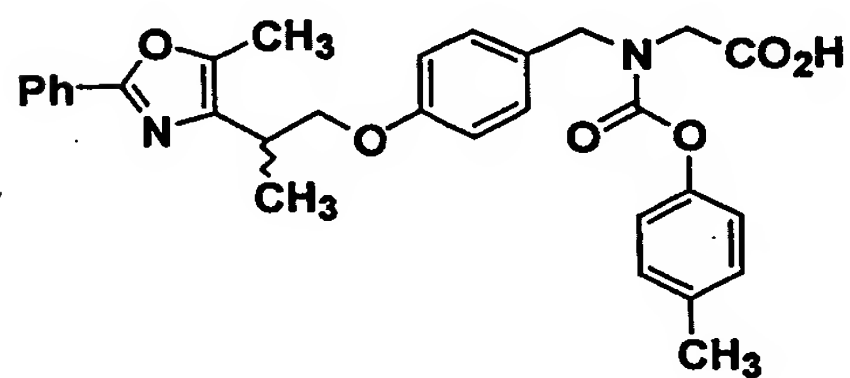
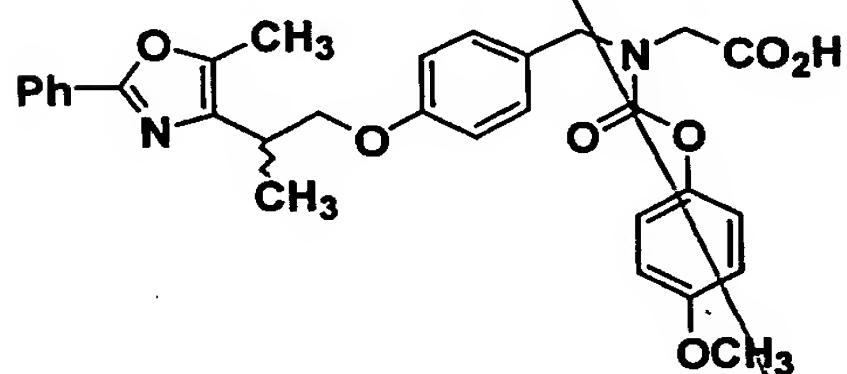
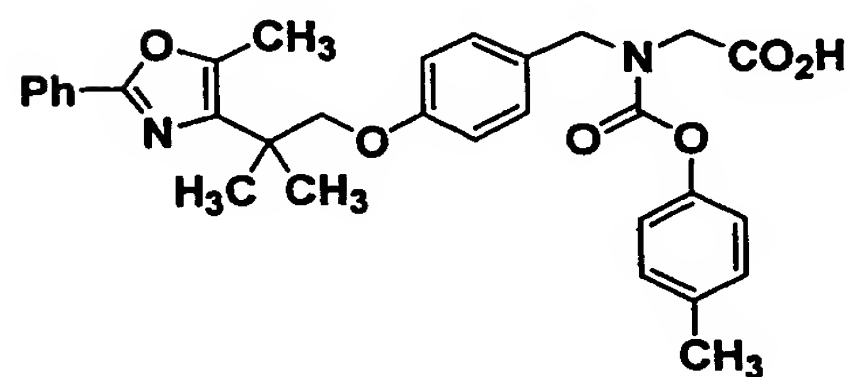
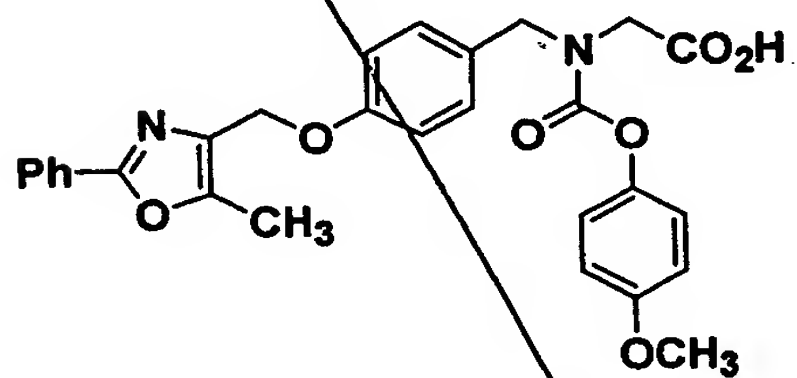
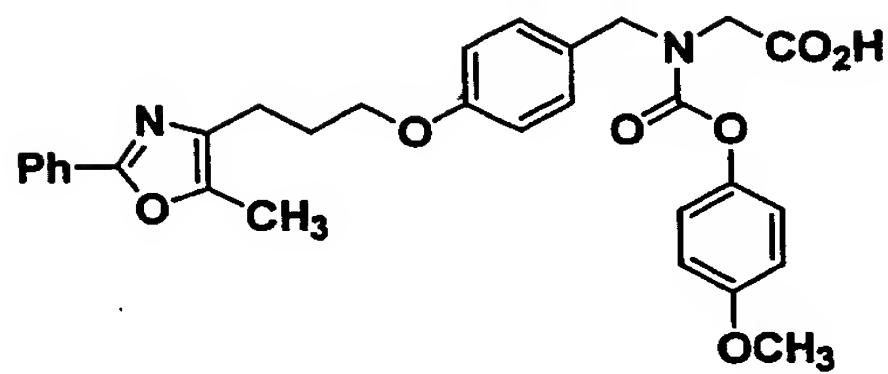
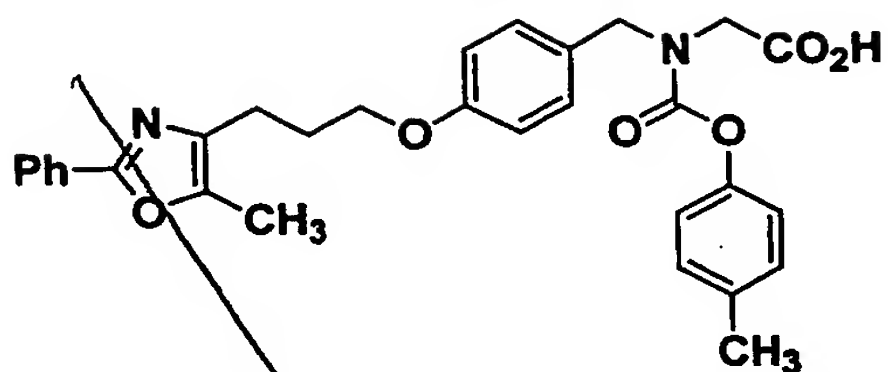
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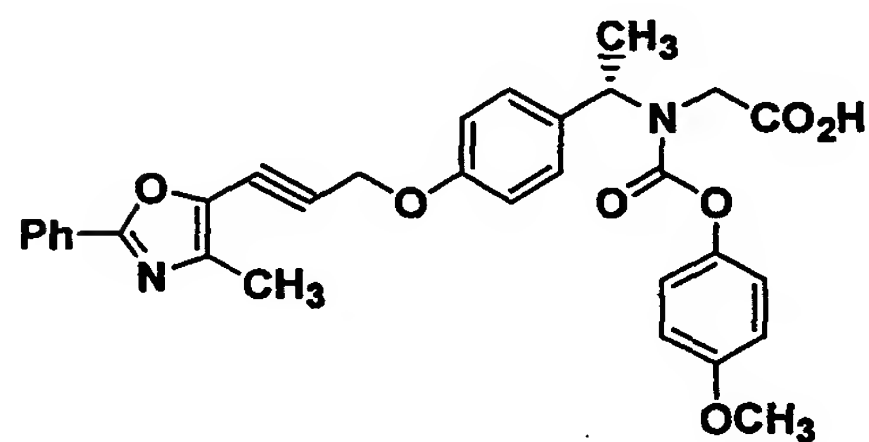
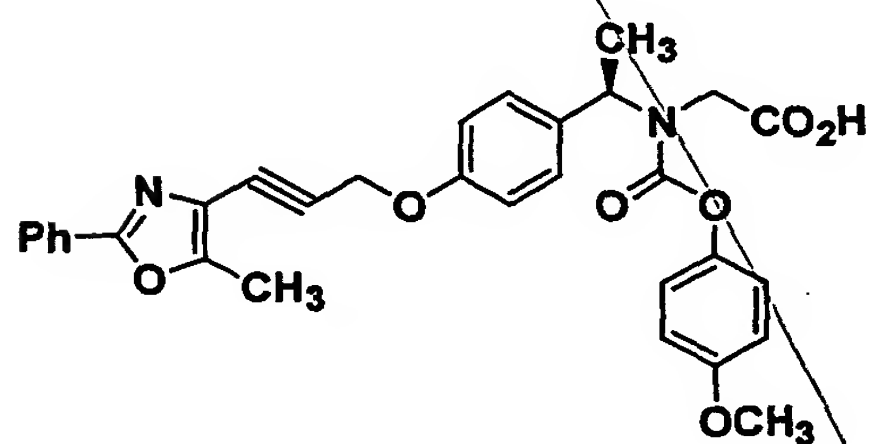
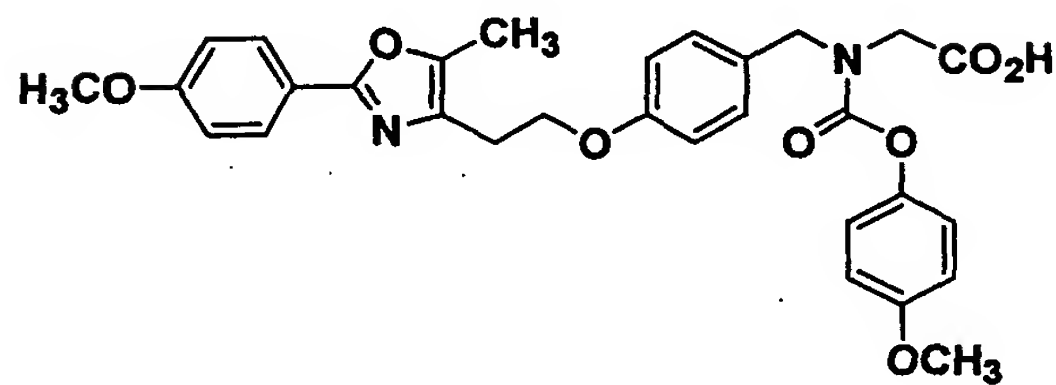
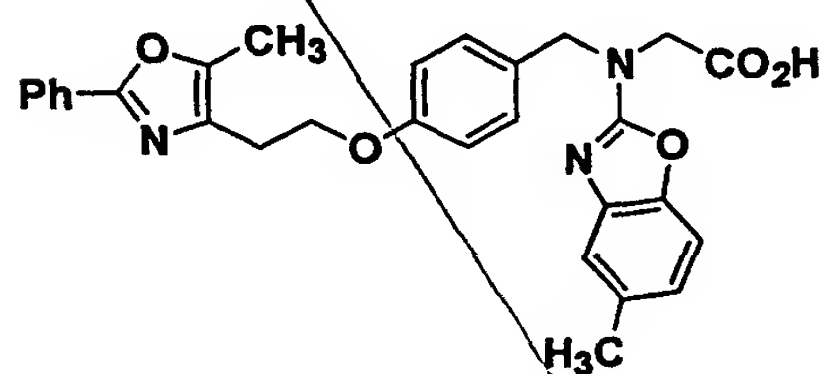
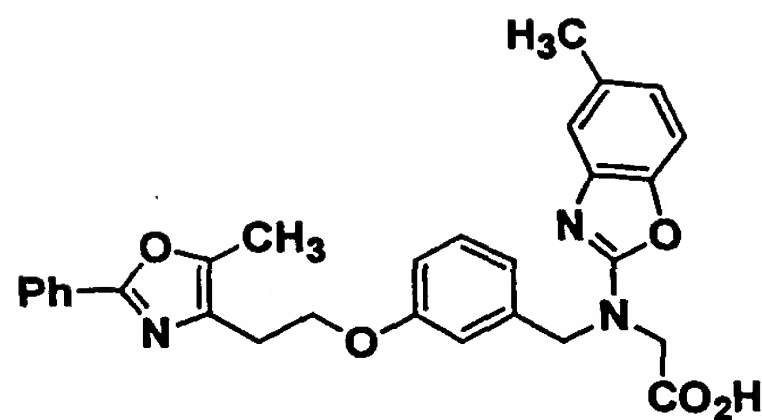
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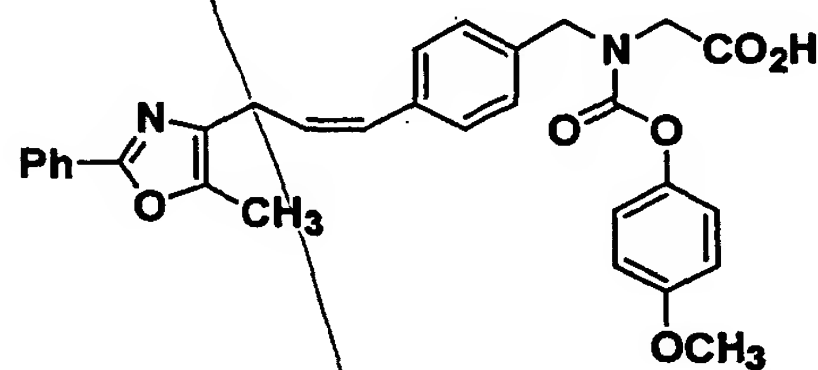
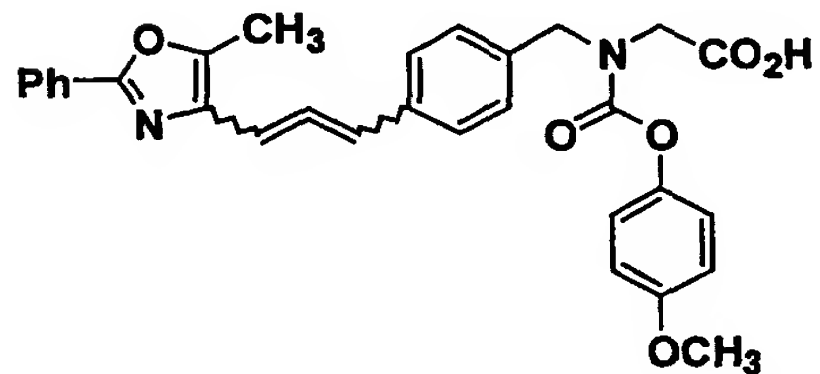
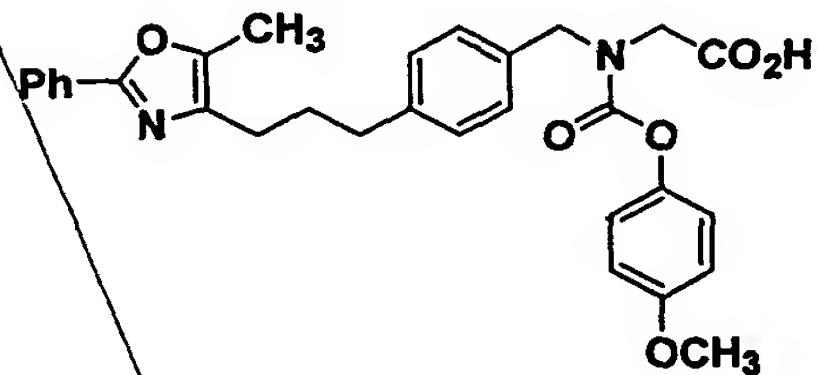
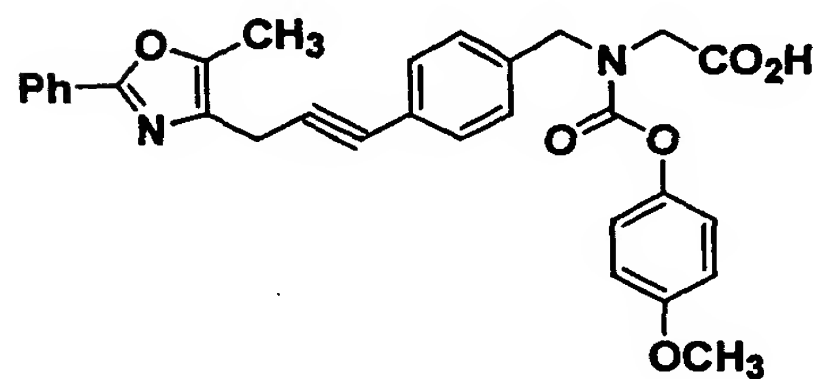
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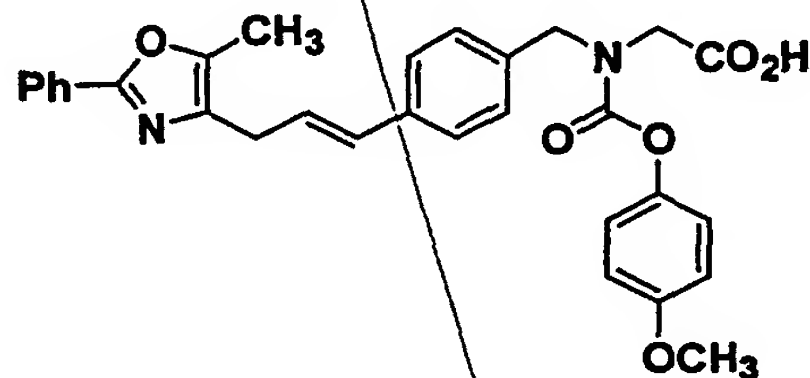
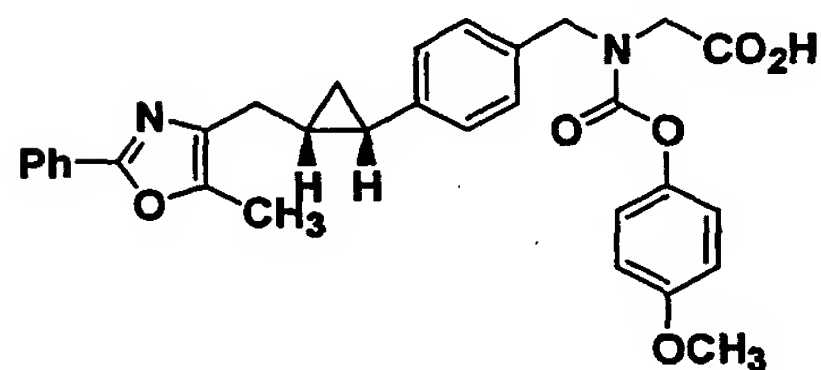
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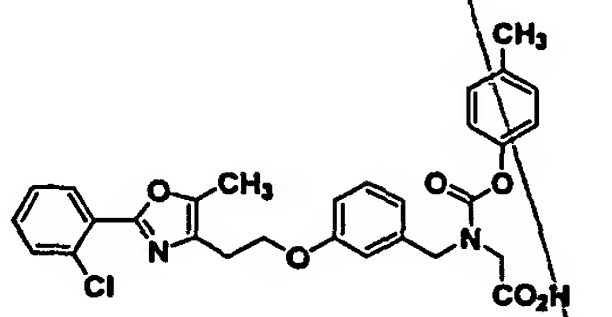
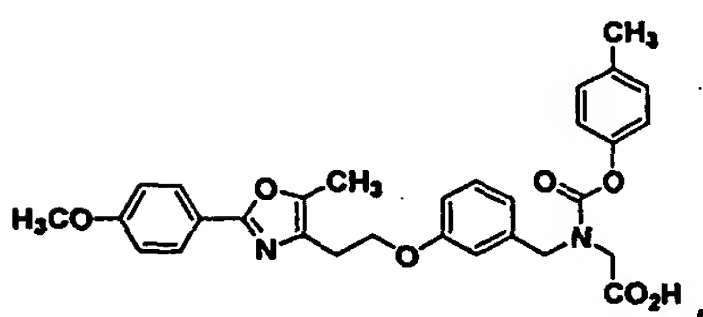
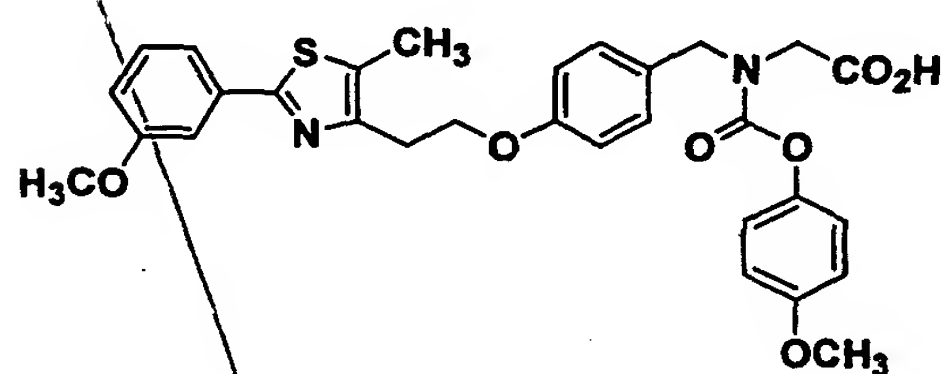
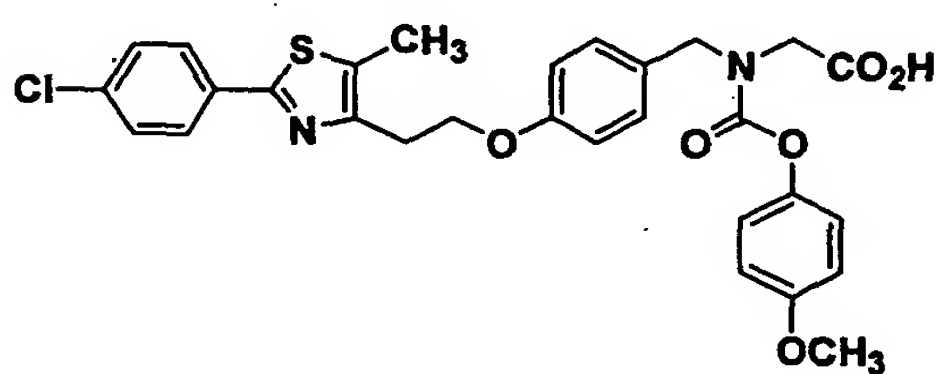
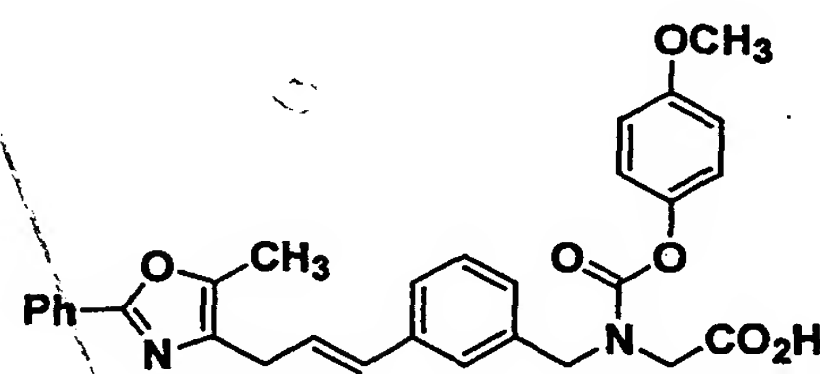
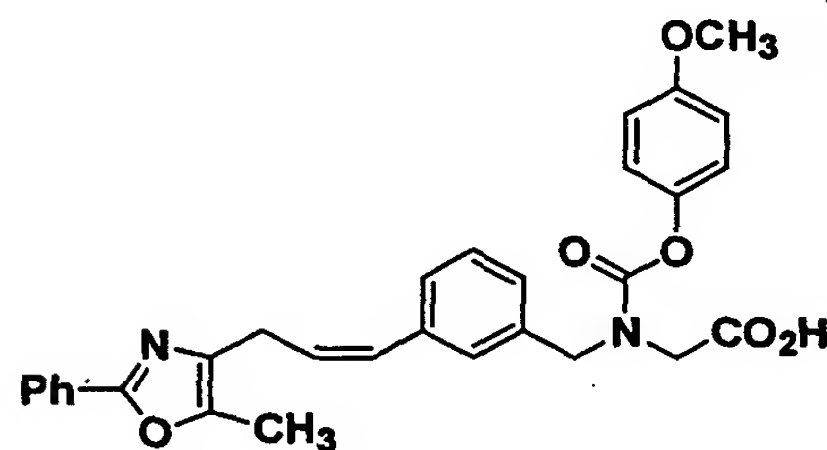
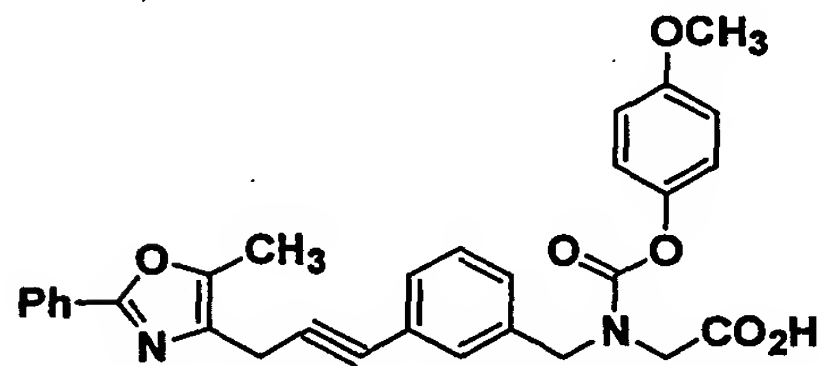
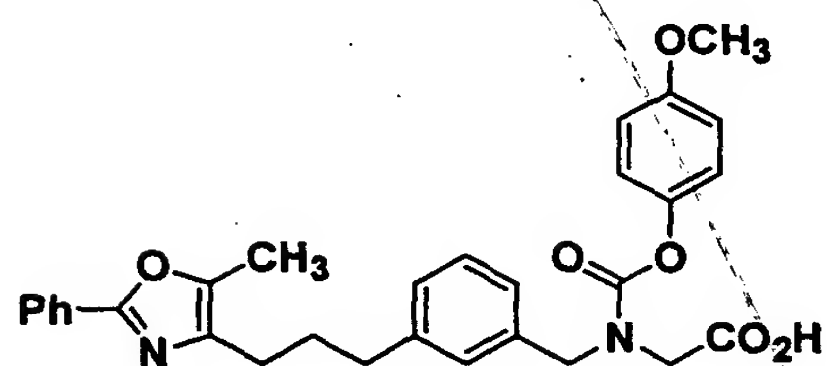
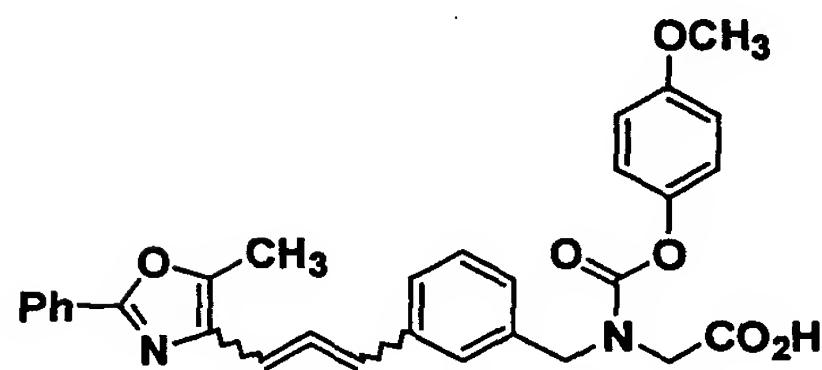
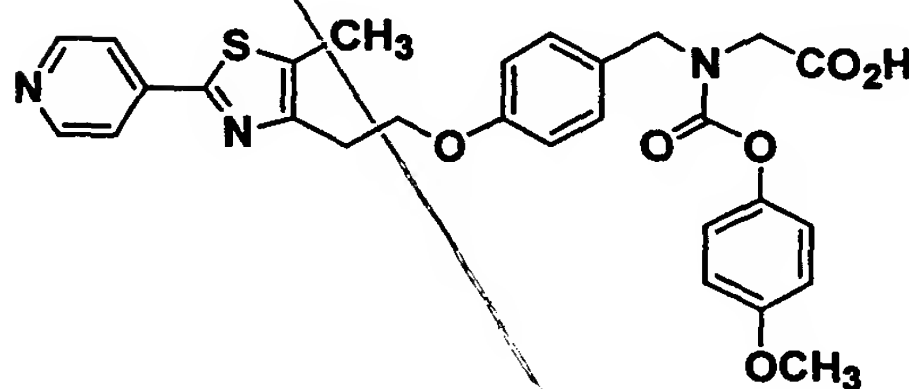
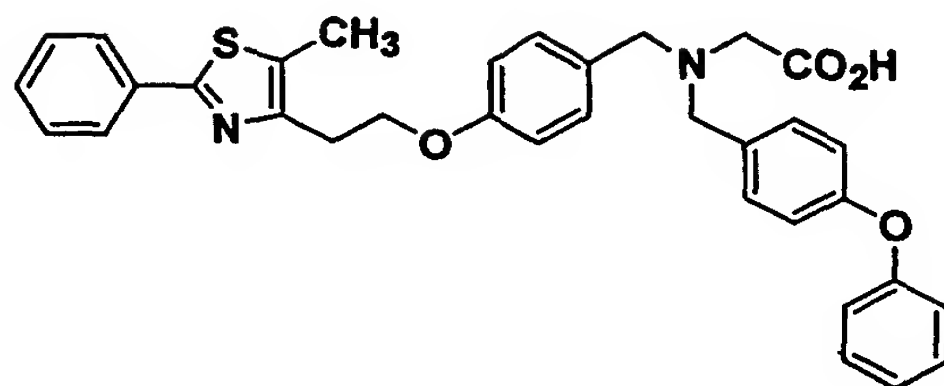
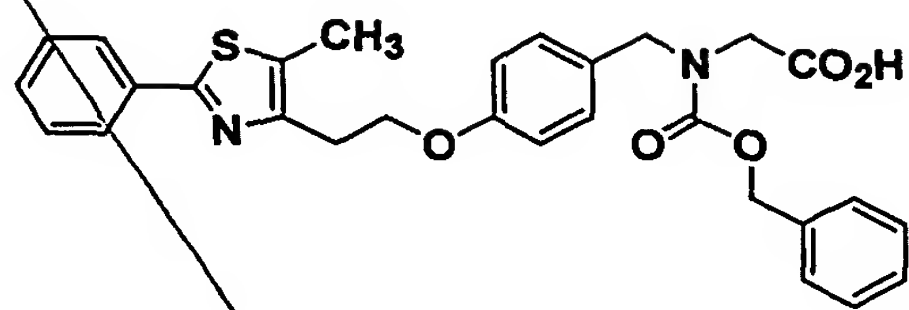


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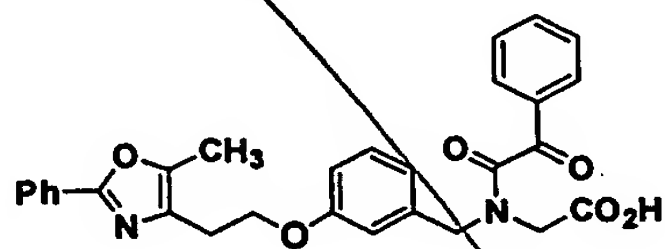
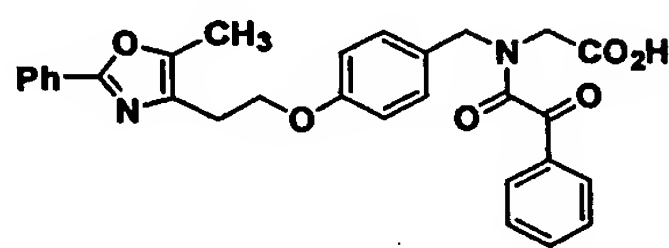




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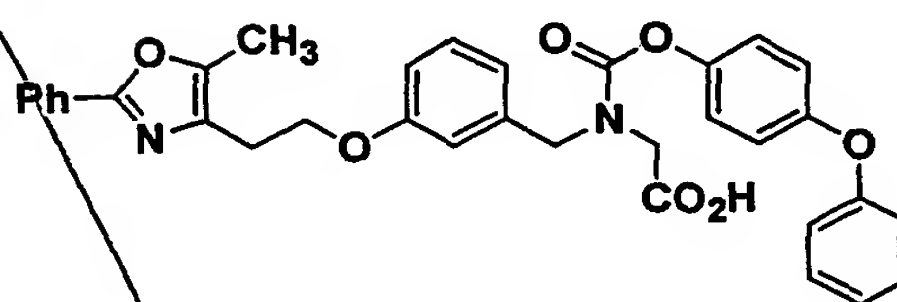
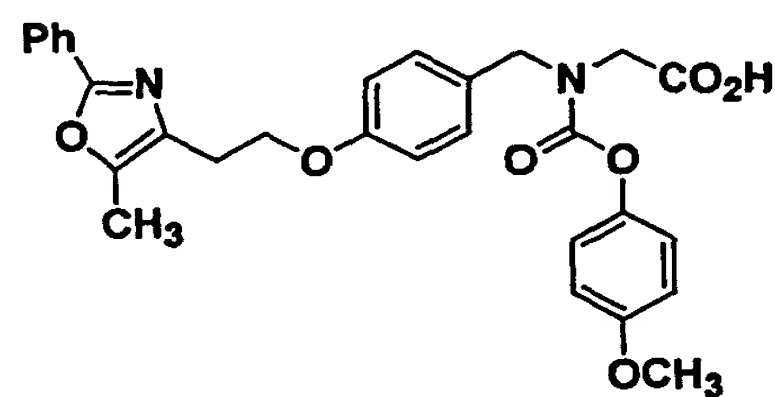
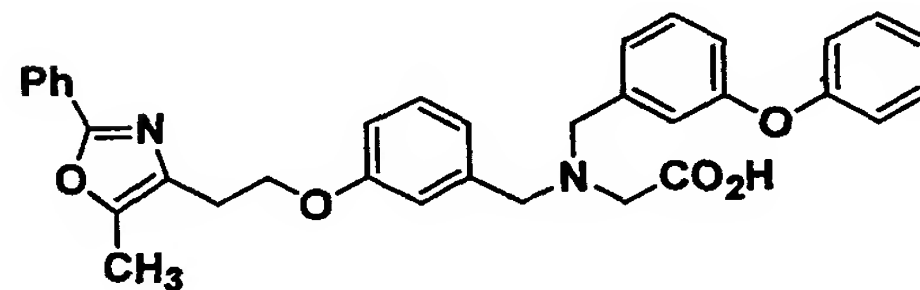
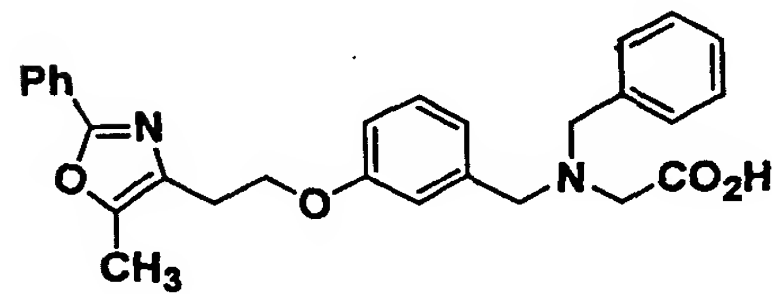
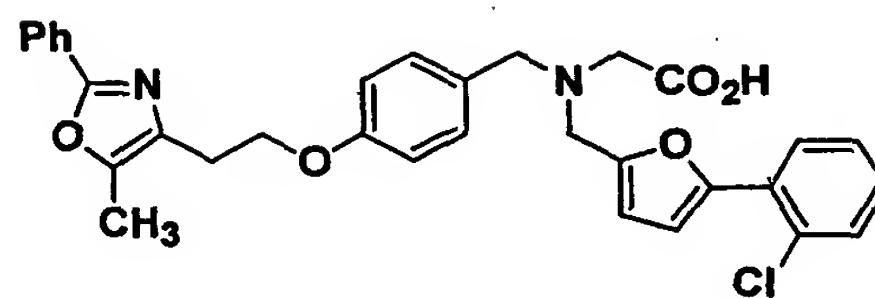
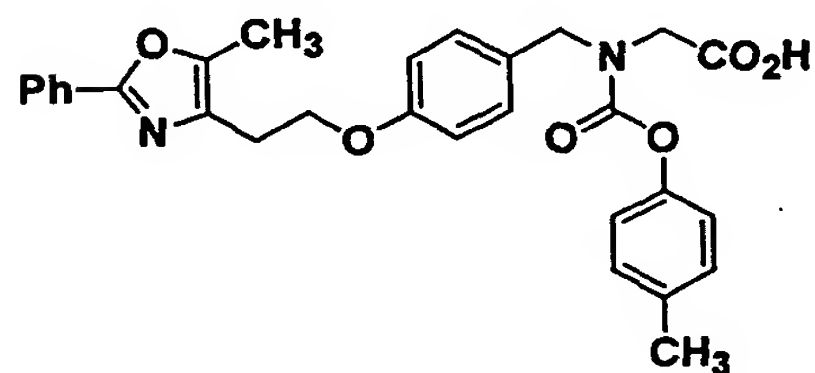
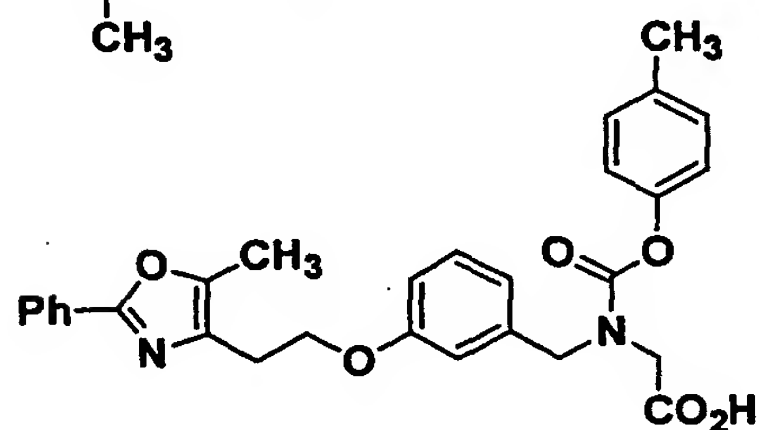
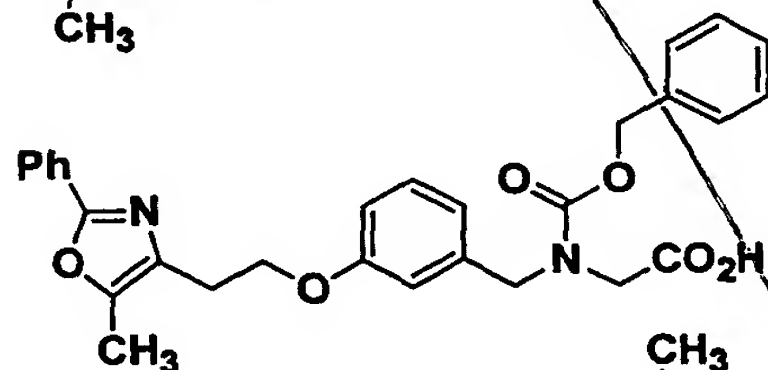
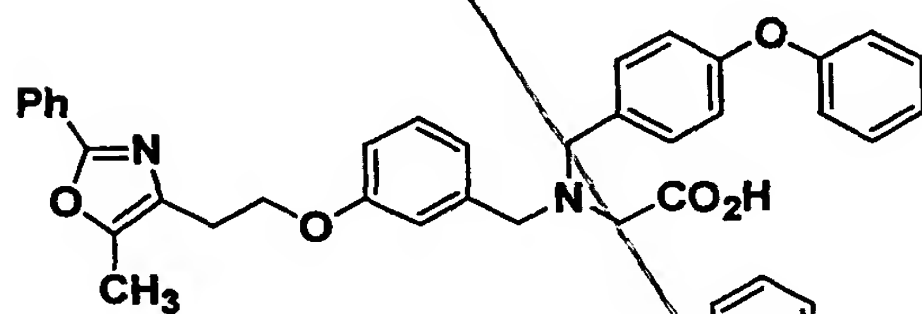
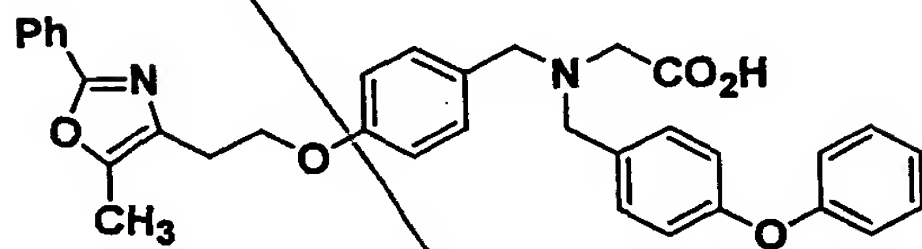
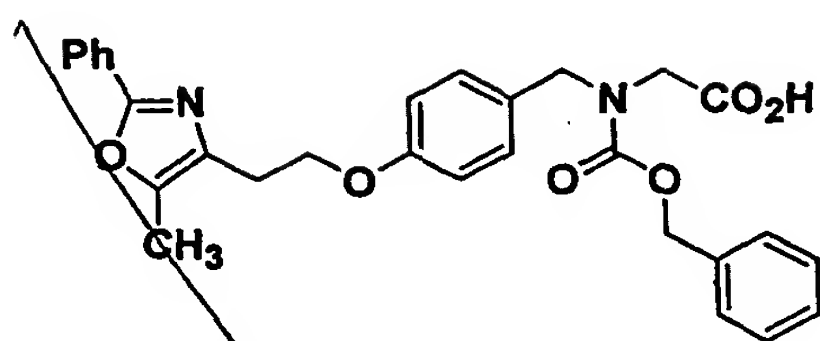
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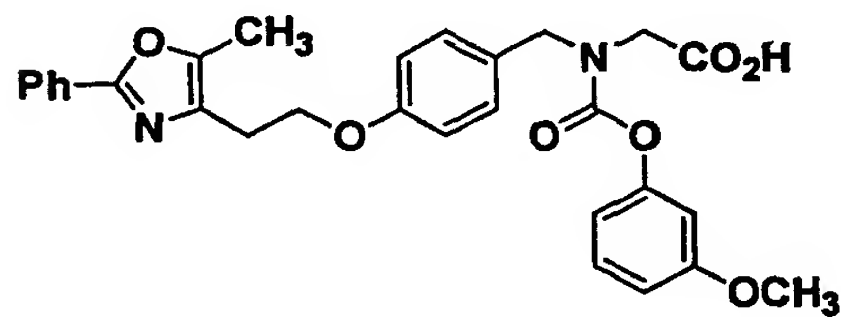
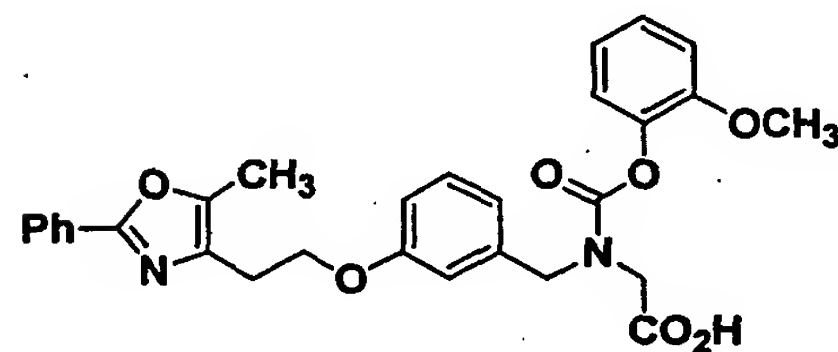
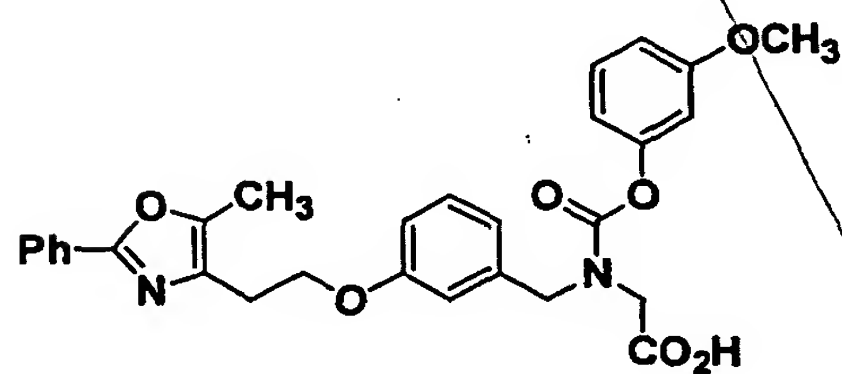
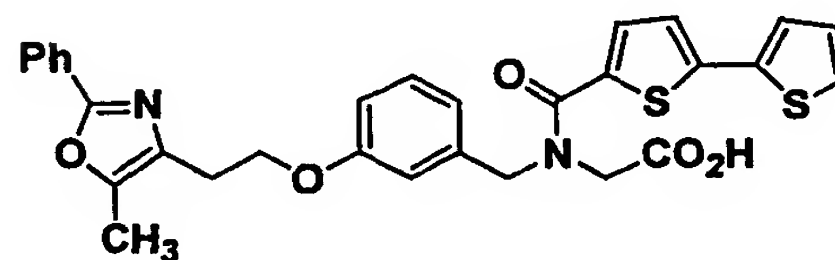
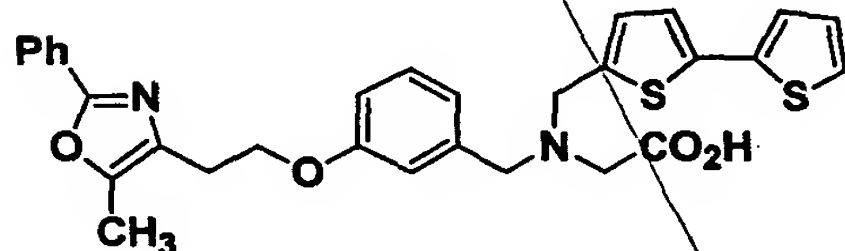
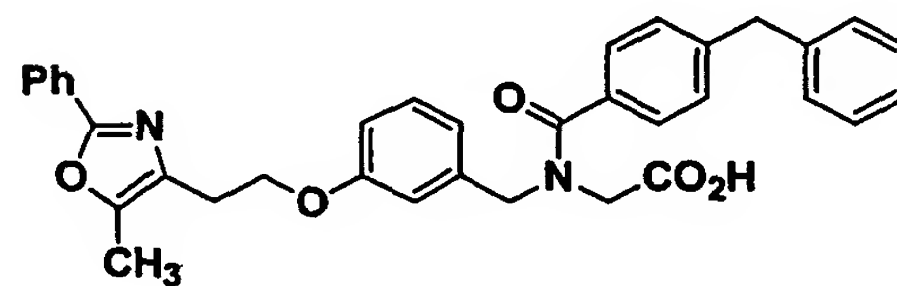
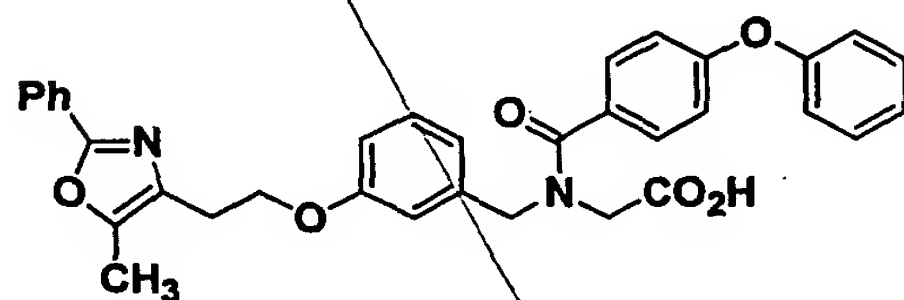
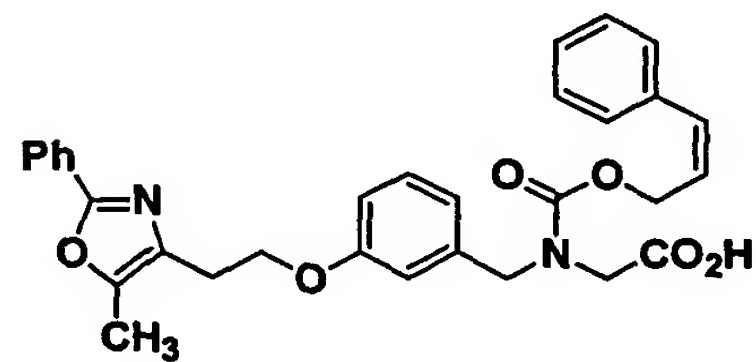
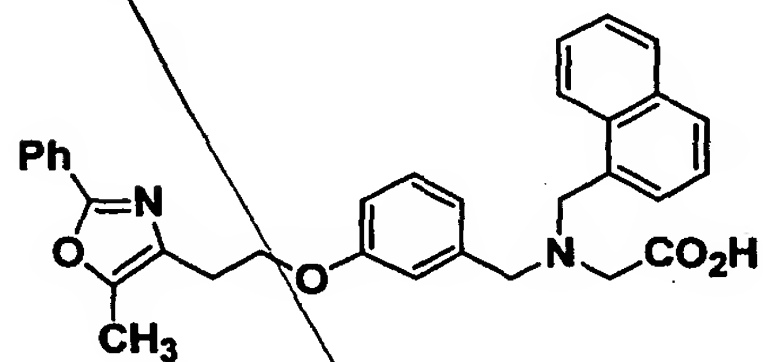
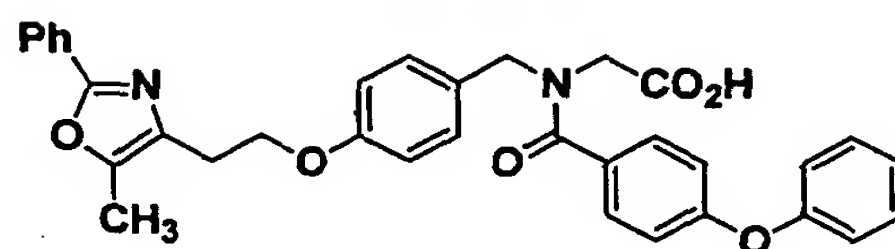
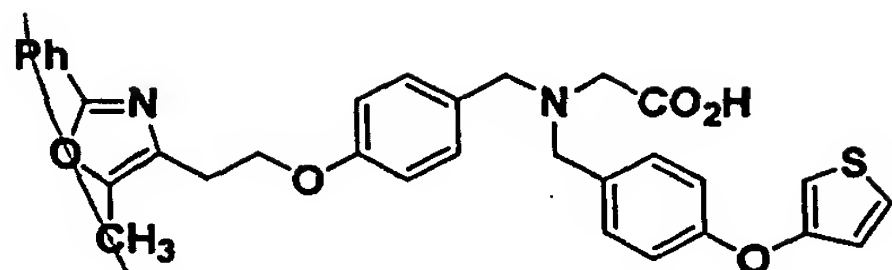
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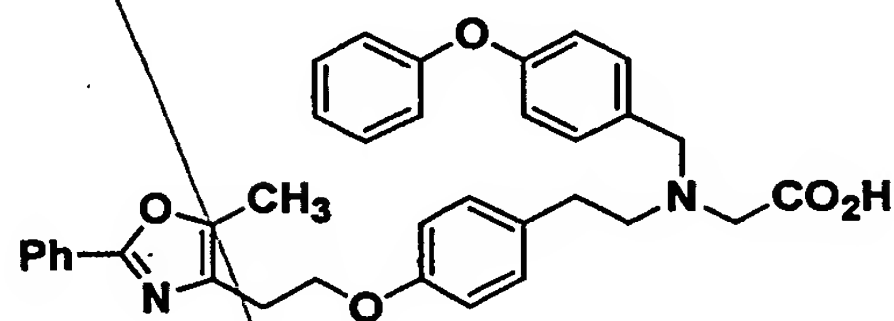
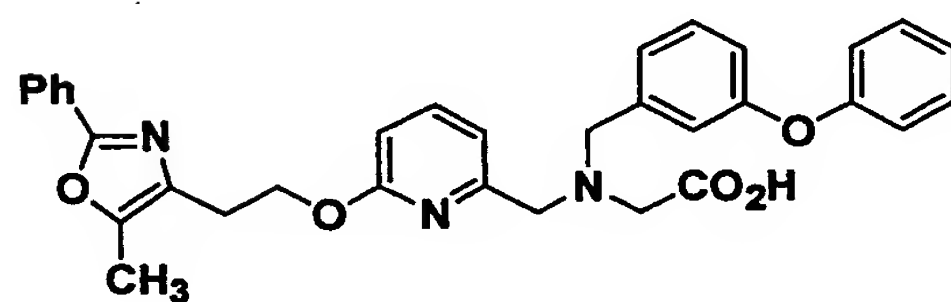
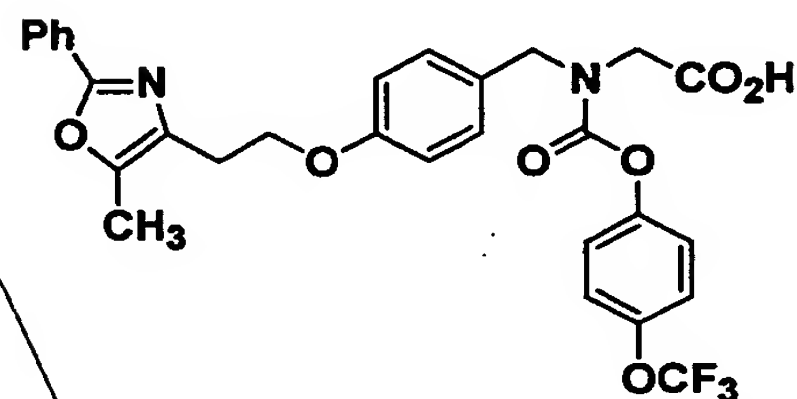
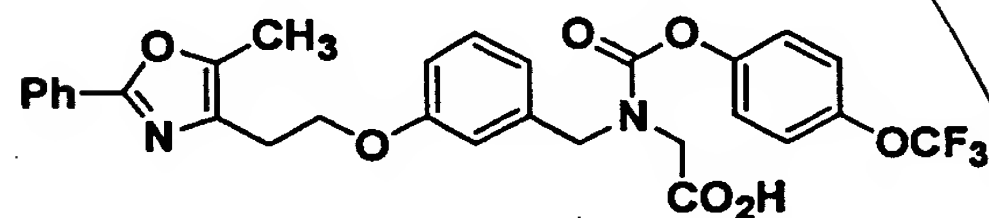
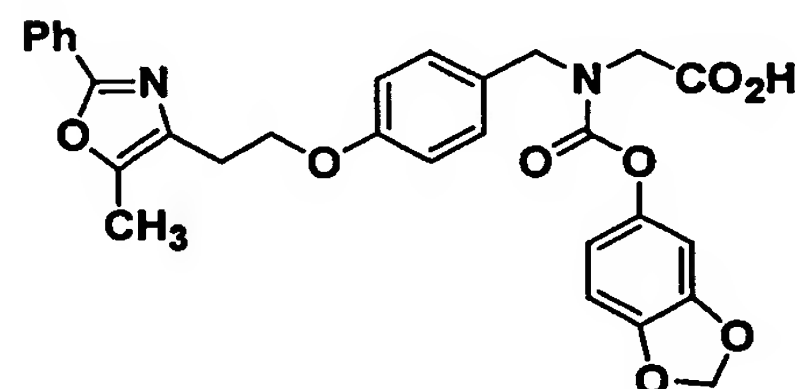
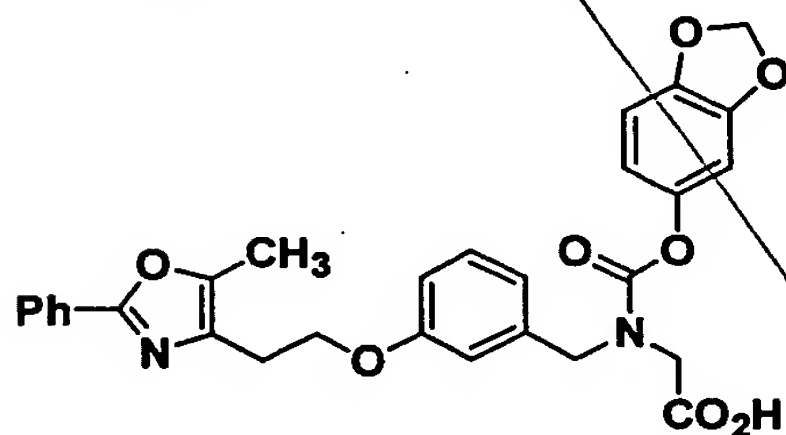
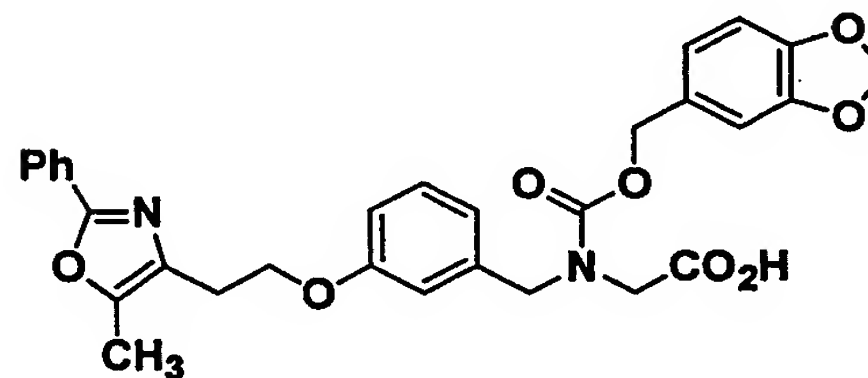
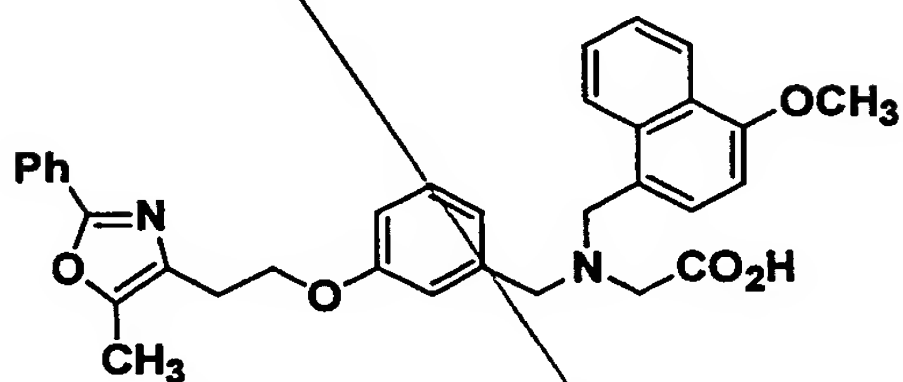
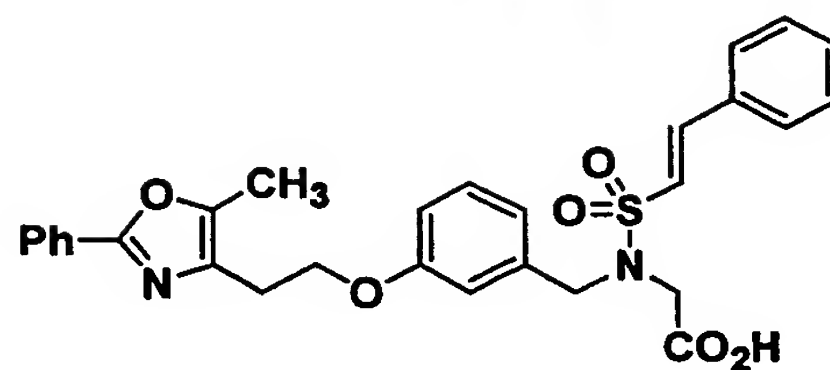
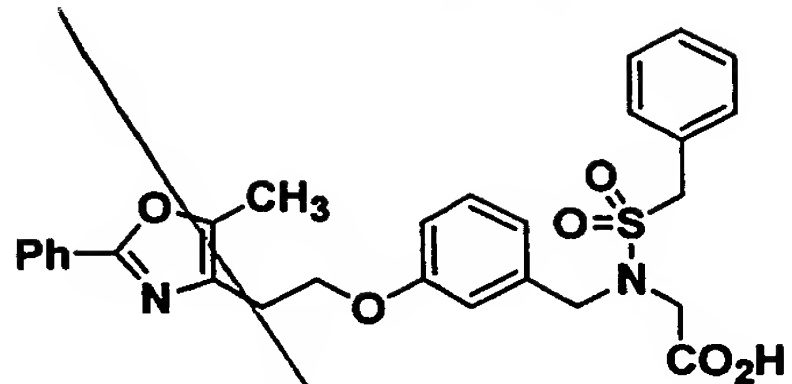
17. The compound as defined in Claim 1 having the structure

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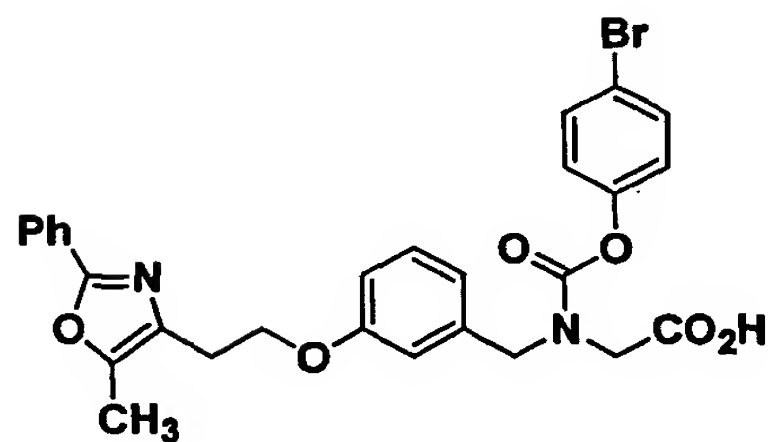
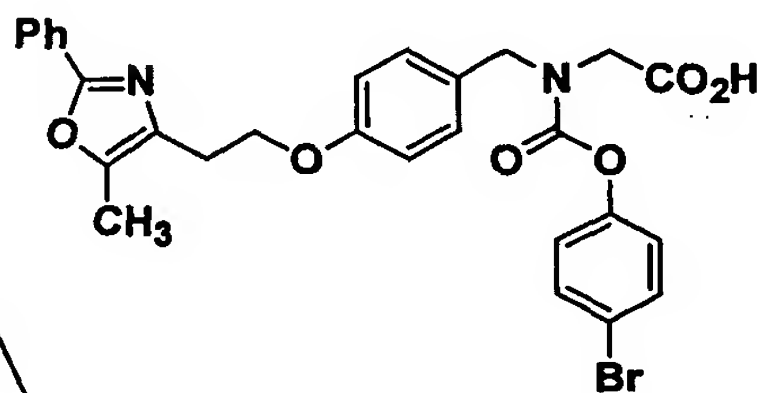
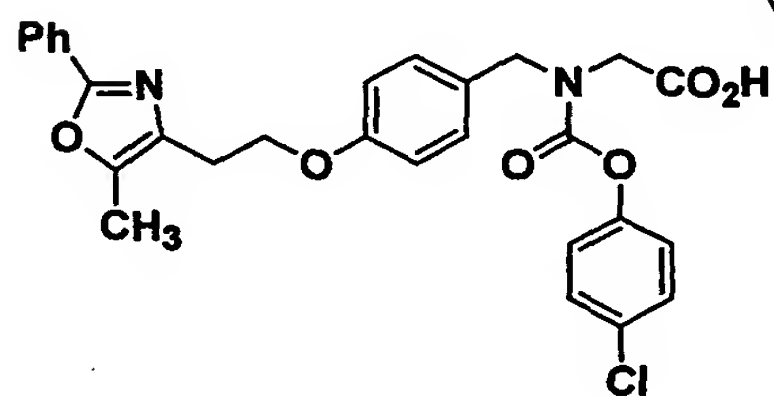
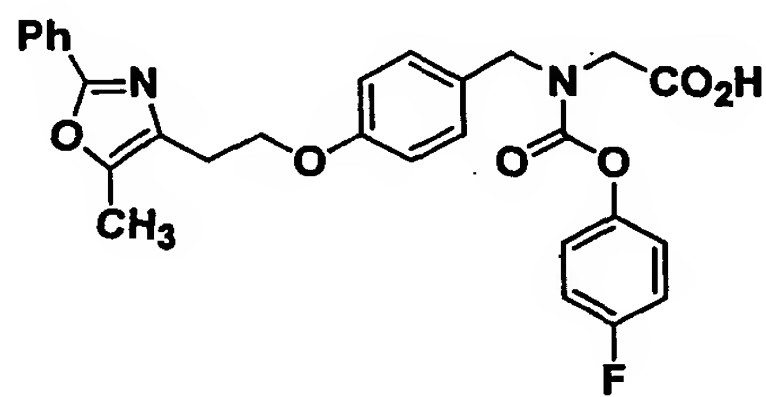
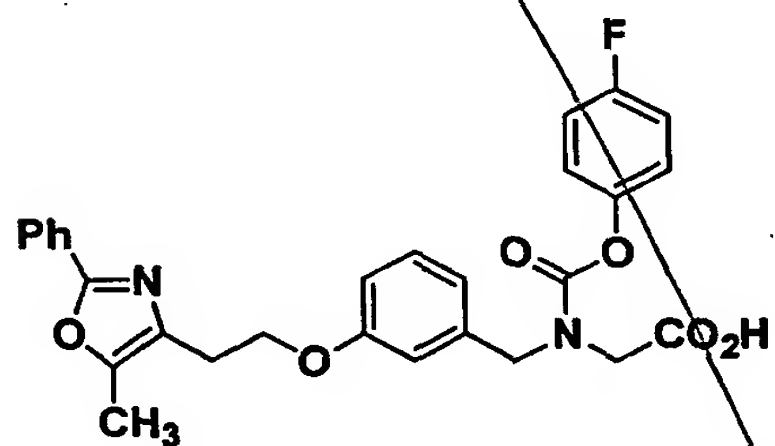
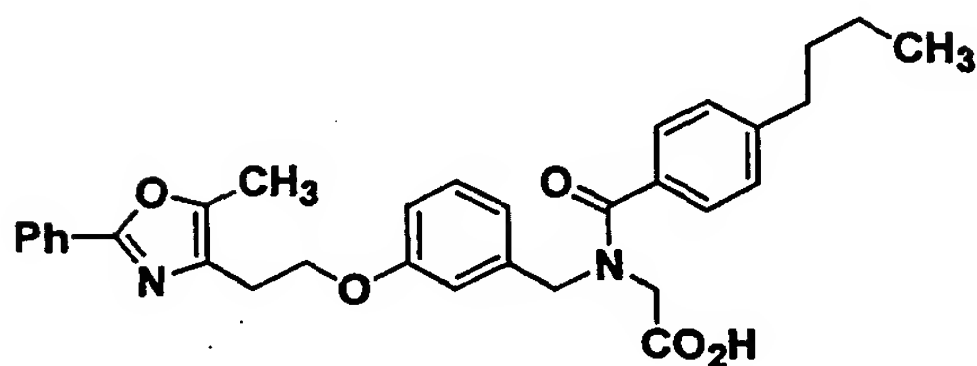
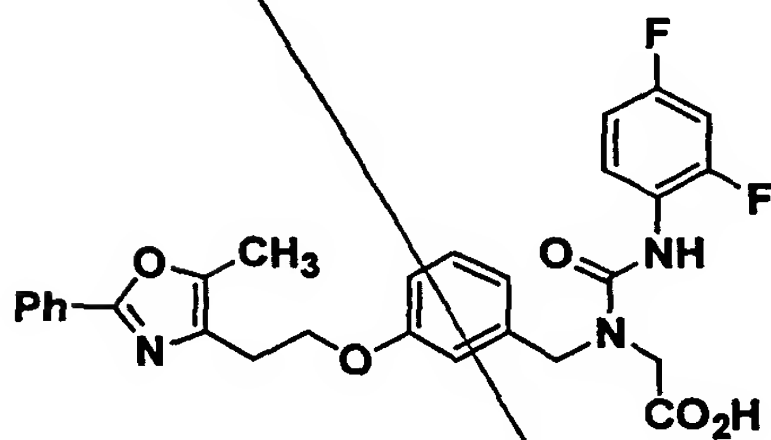
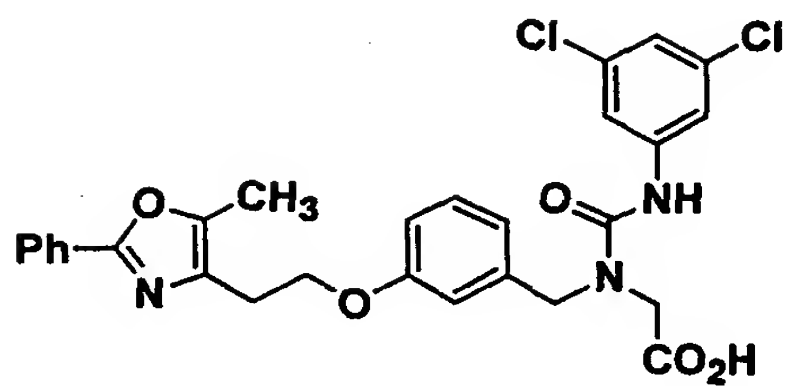
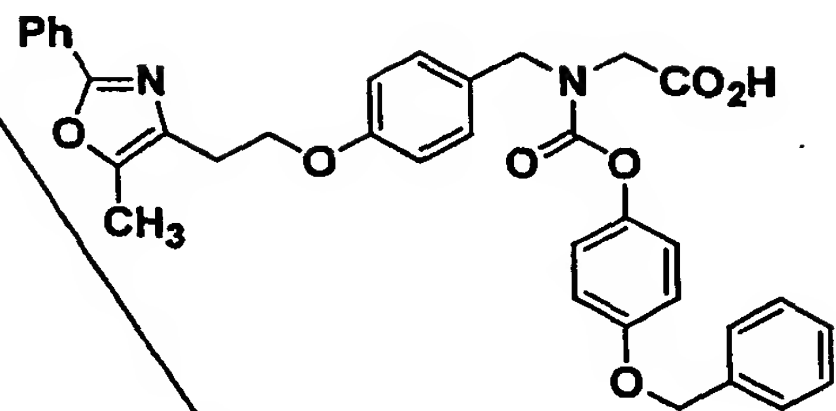




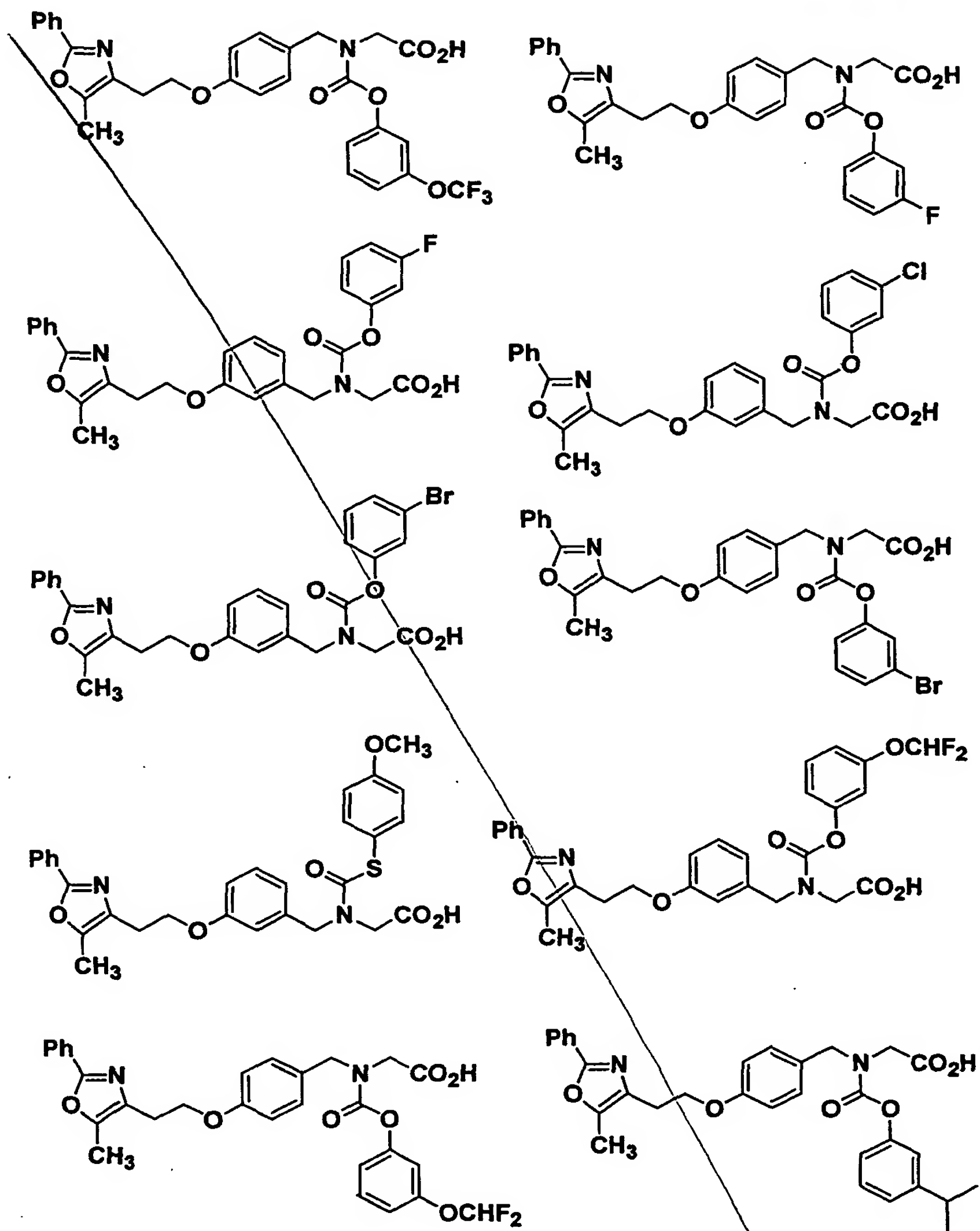
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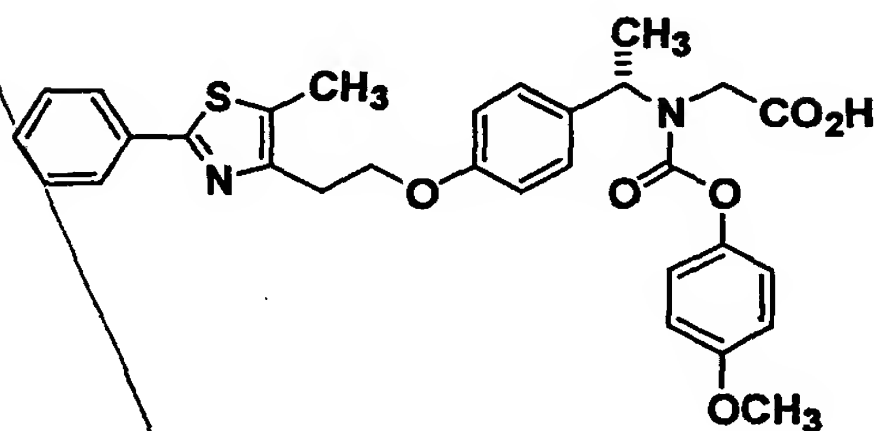
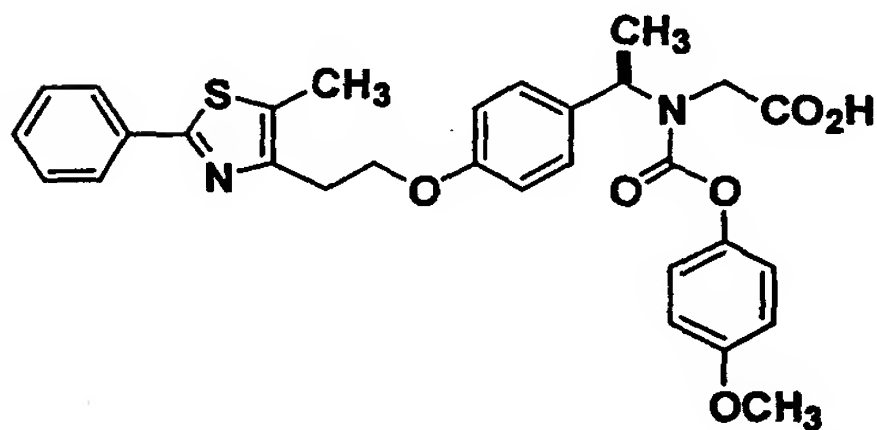
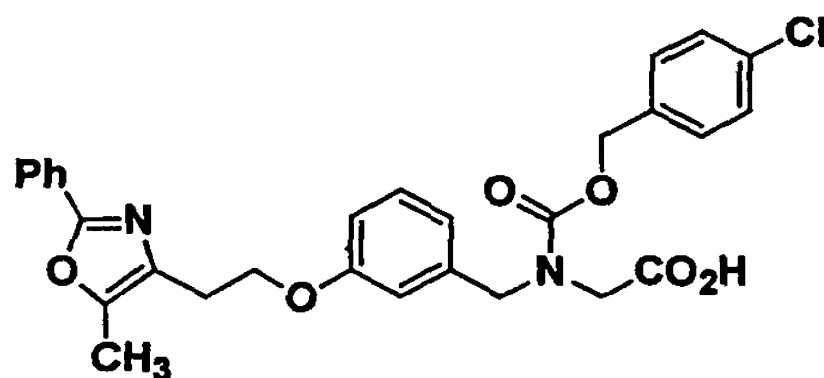
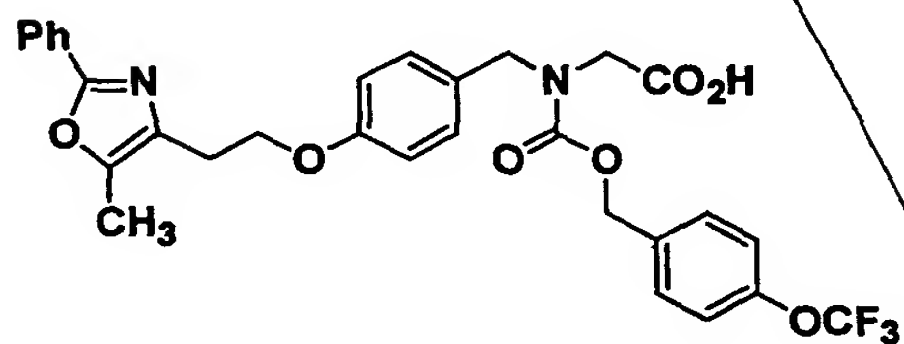
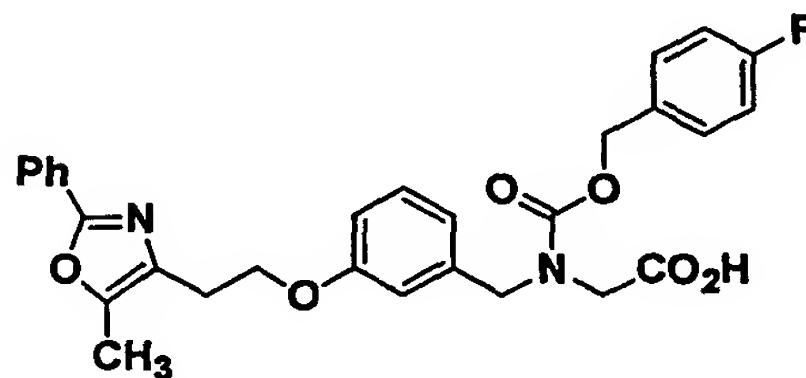
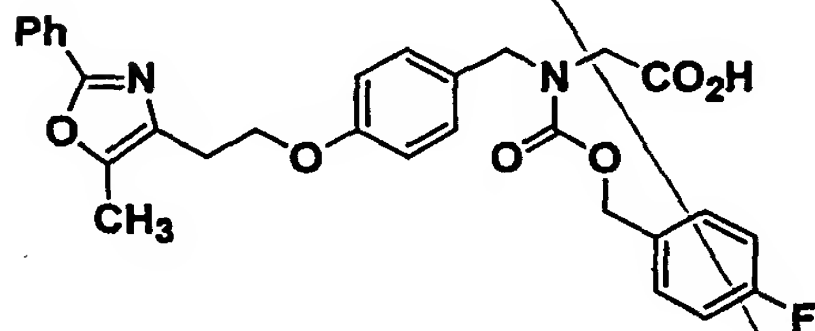
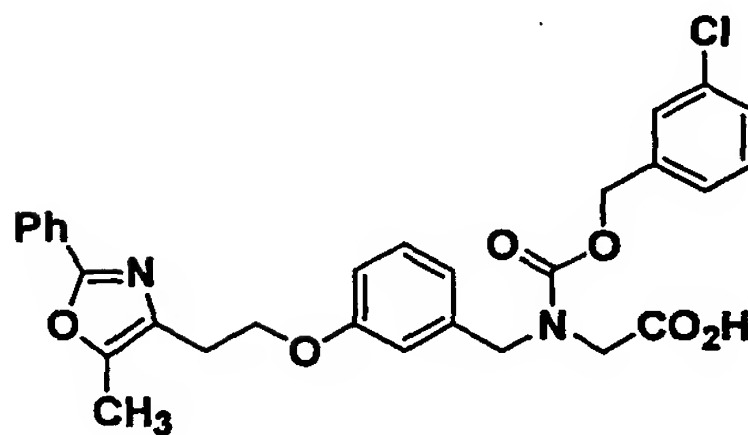
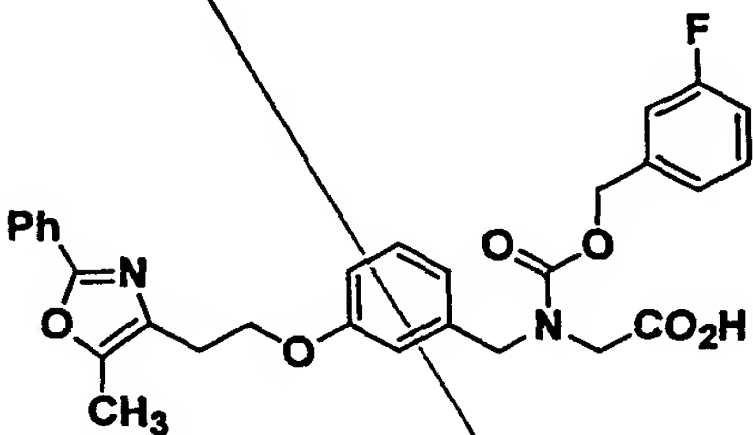
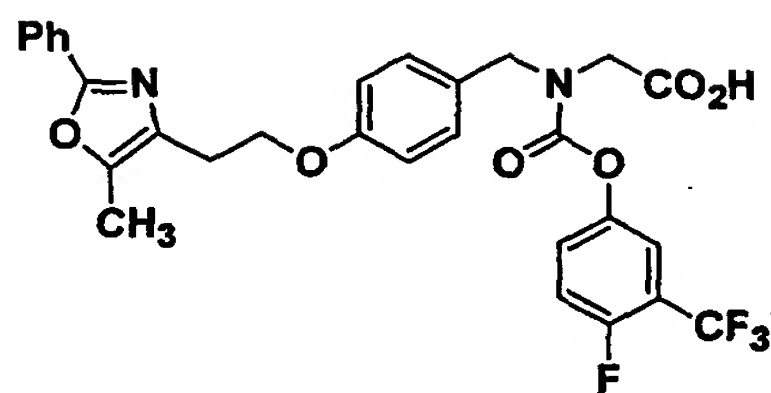
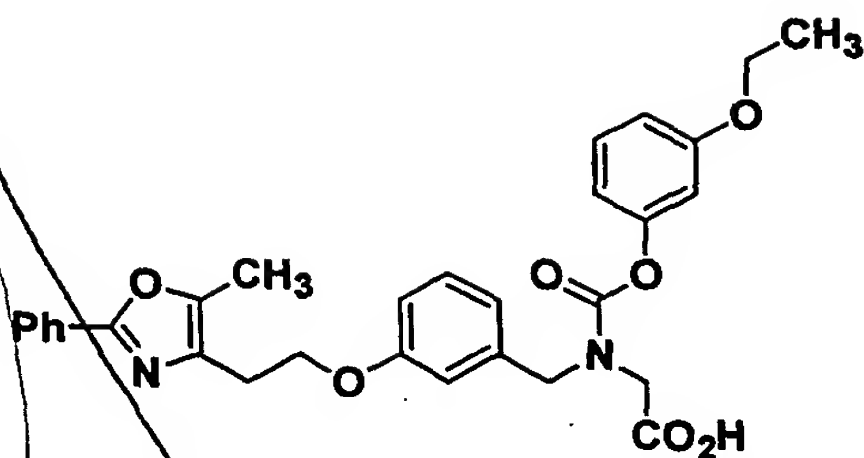
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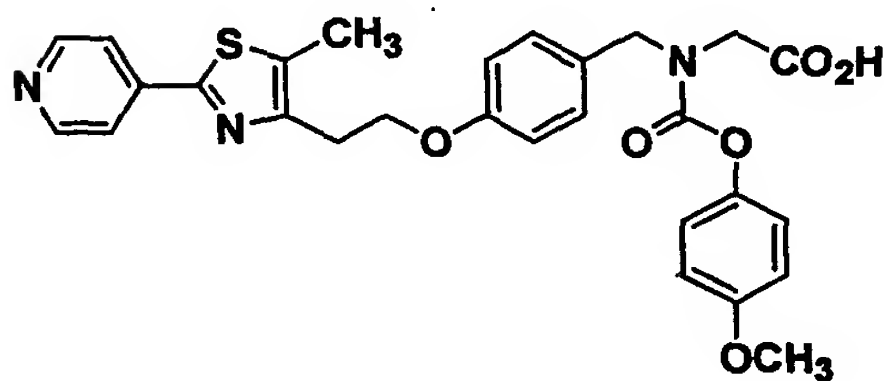
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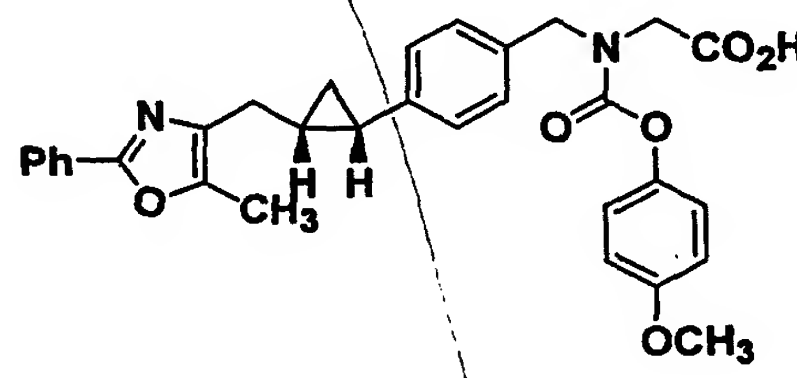
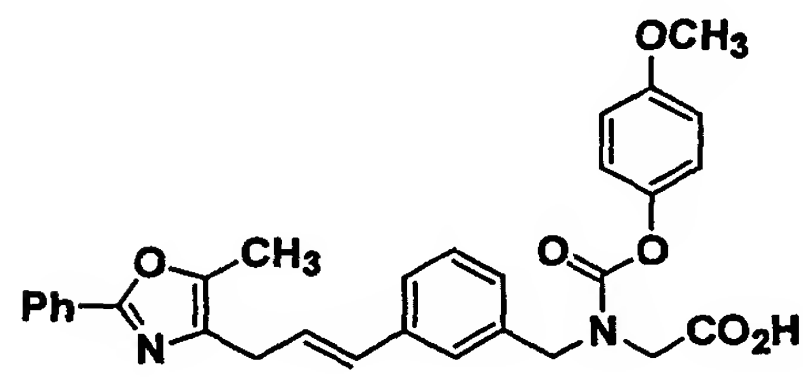
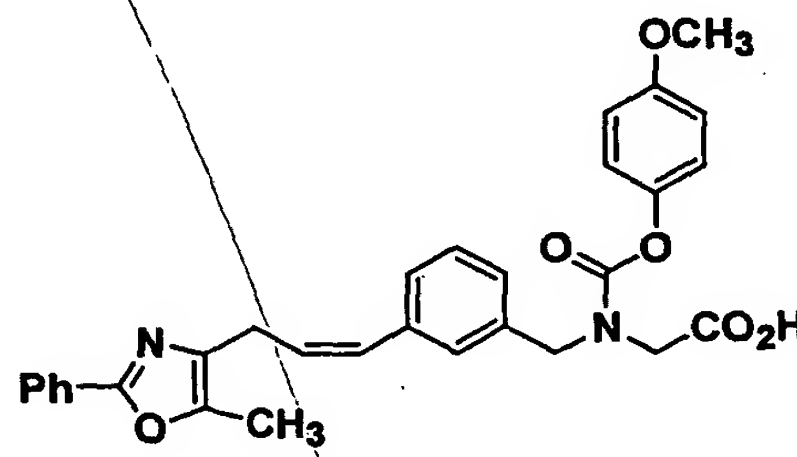
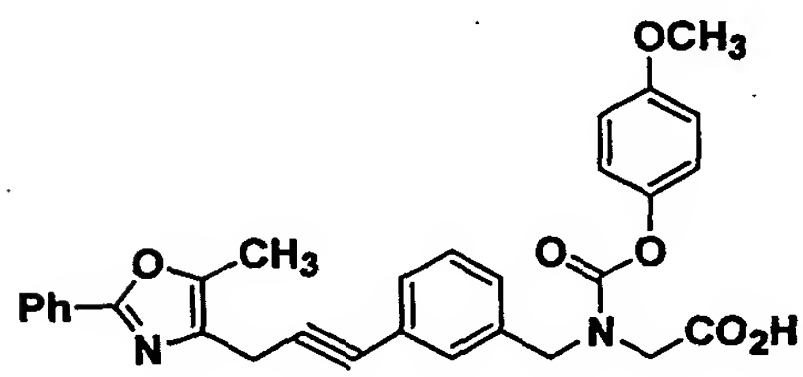
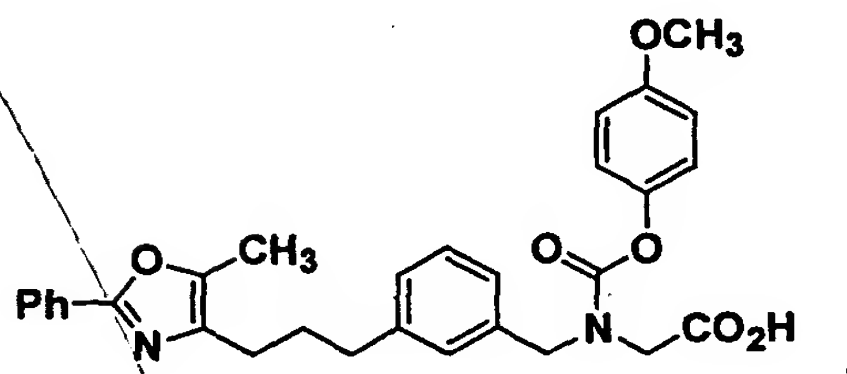
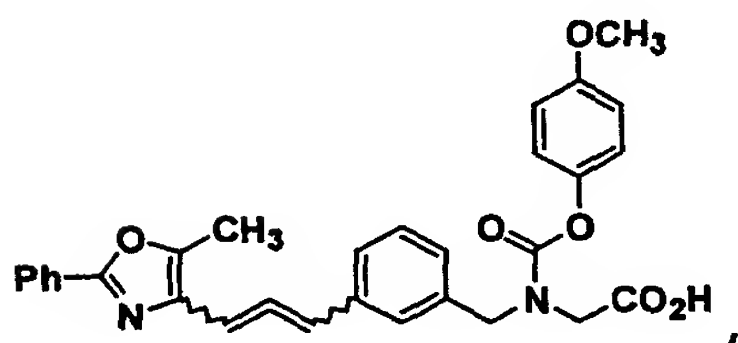
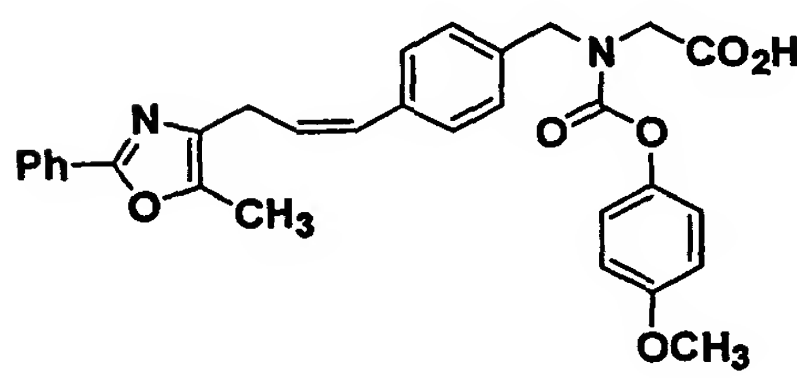
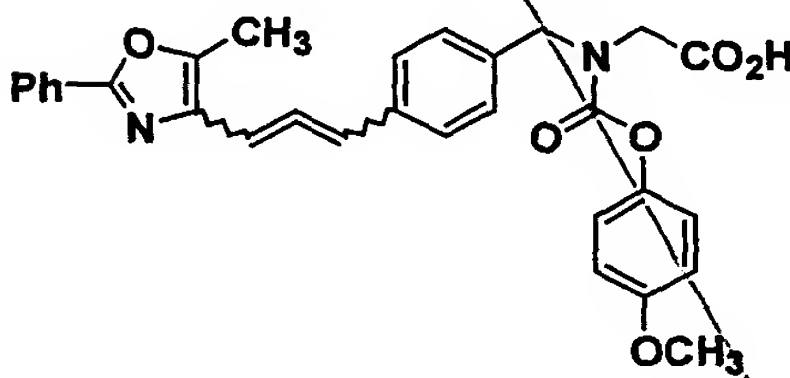
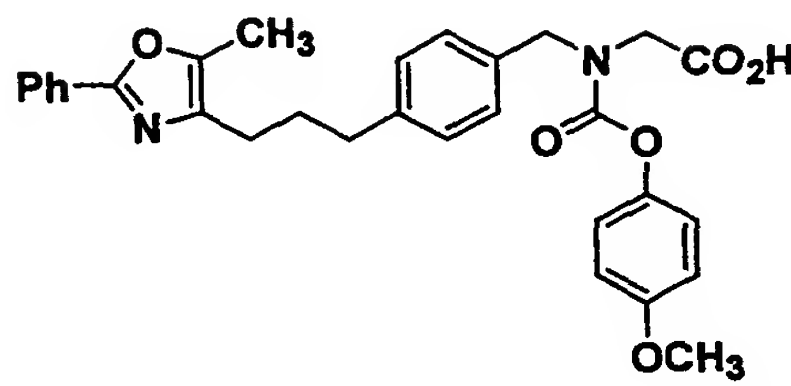
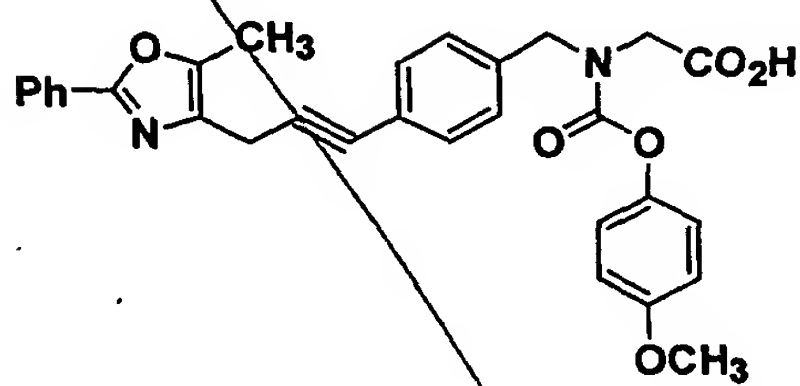
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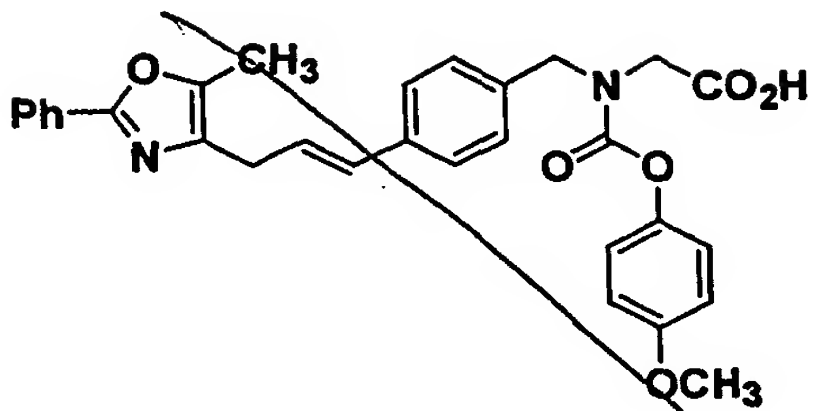
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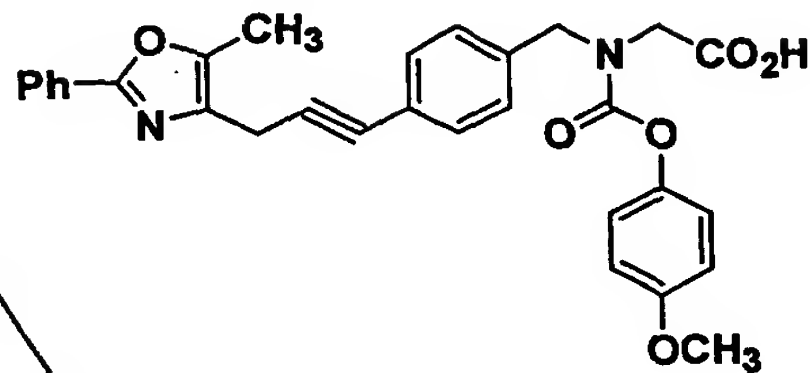
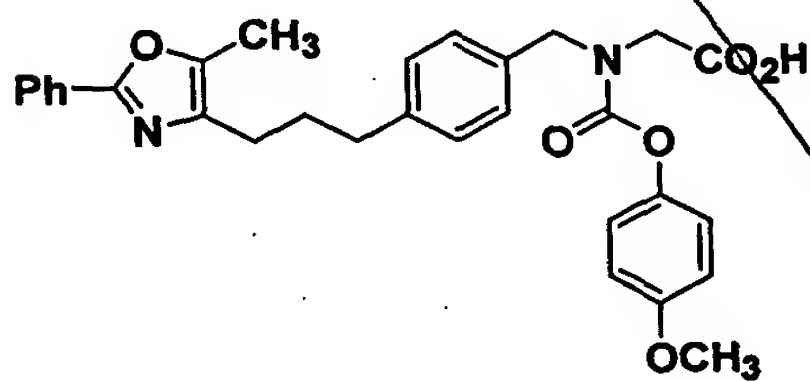
18. The compound as defined in Claim 1 having the structure



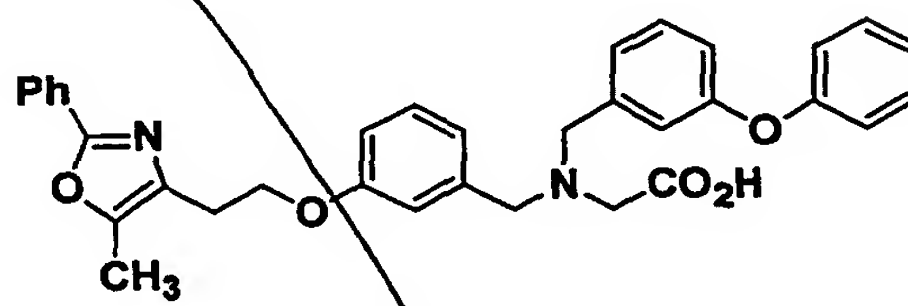
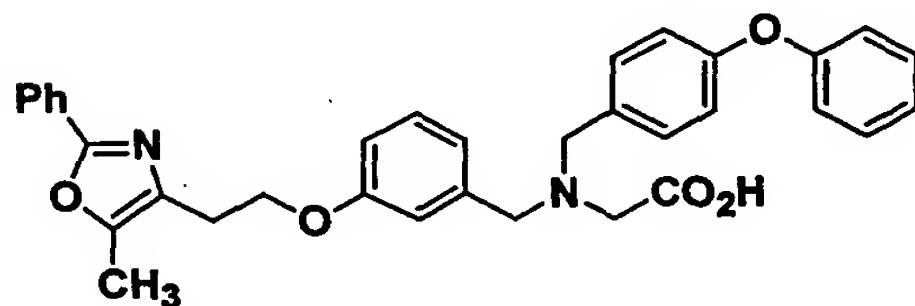
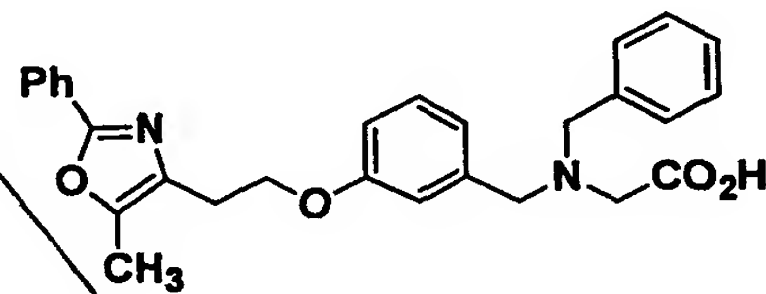
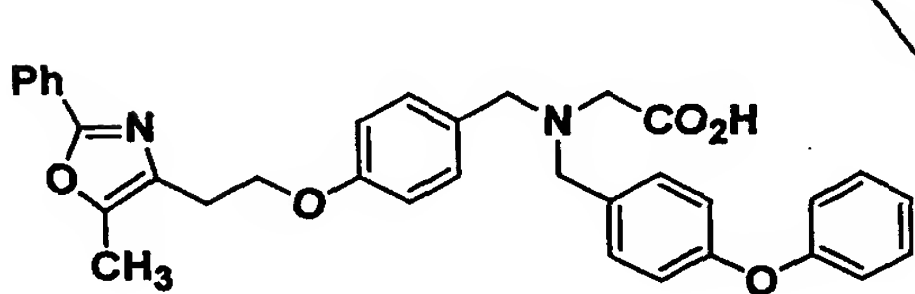
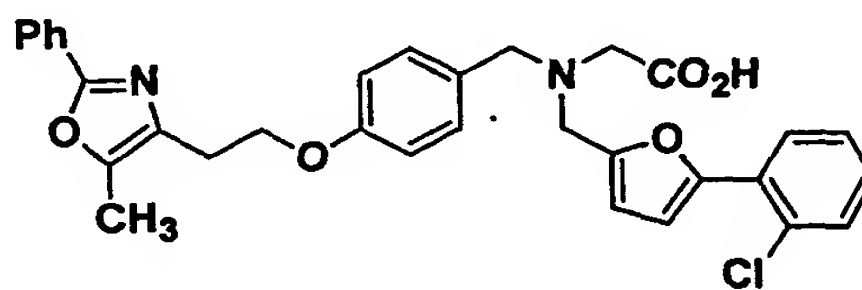
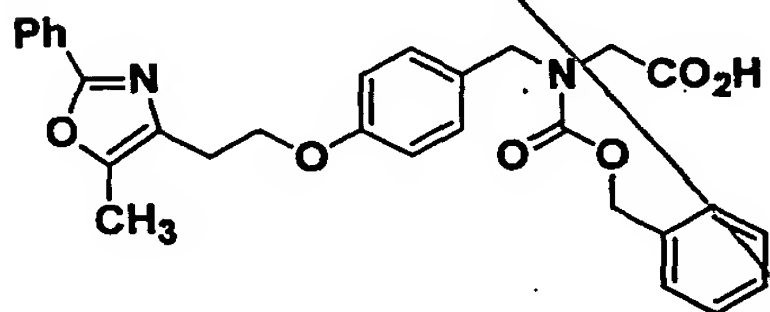
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19. The compound as defined in Claim 1 having the structure

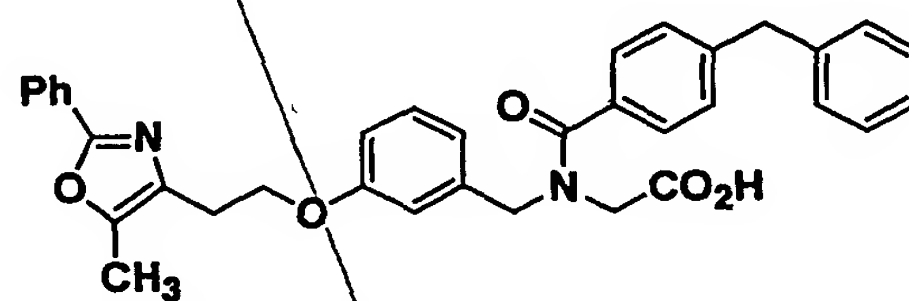
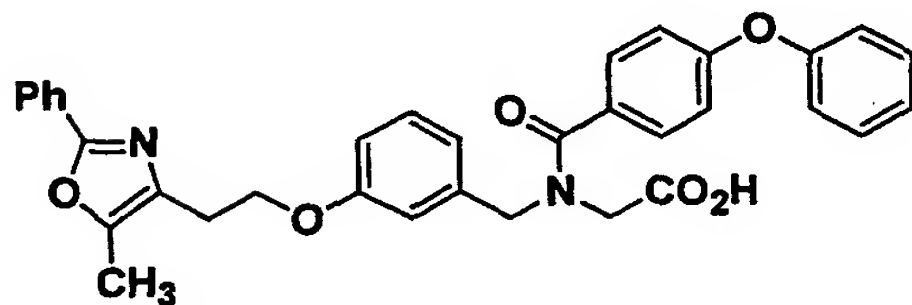
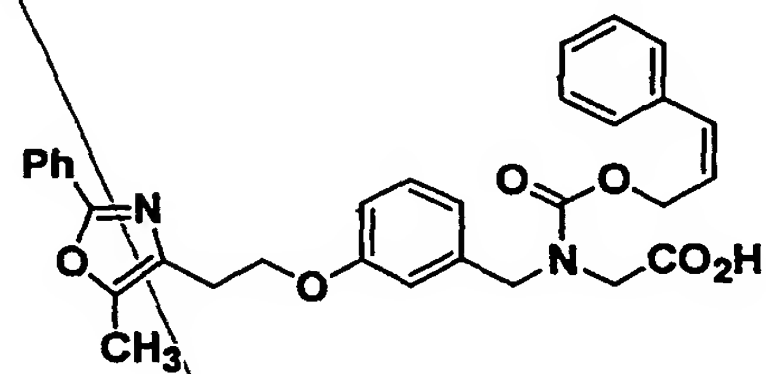
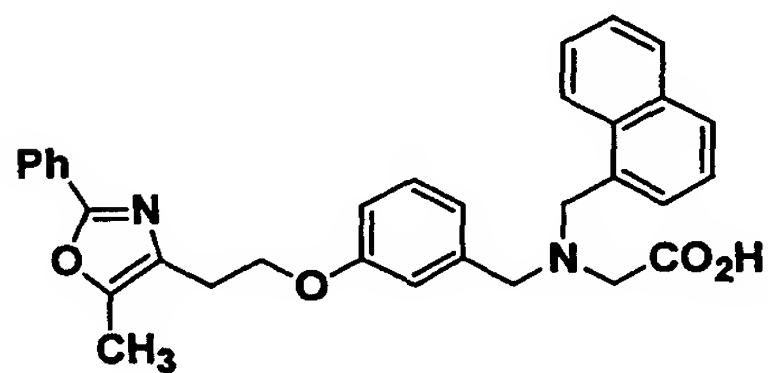
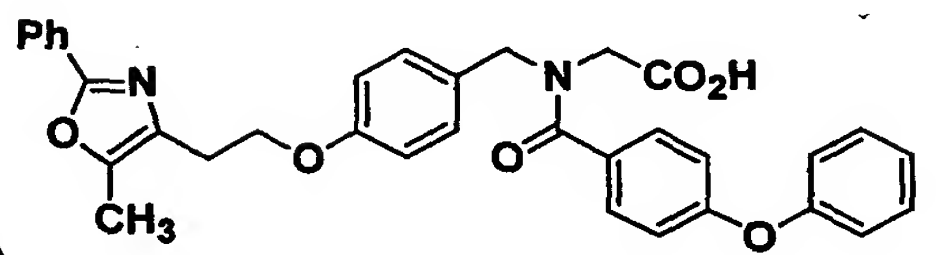
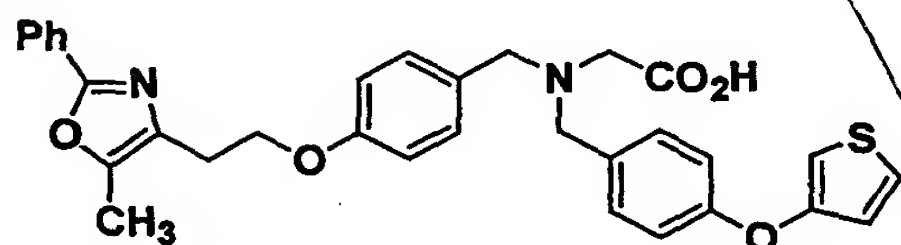
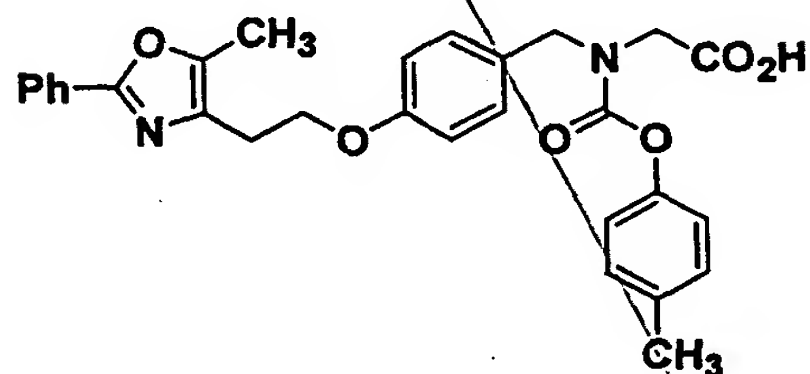
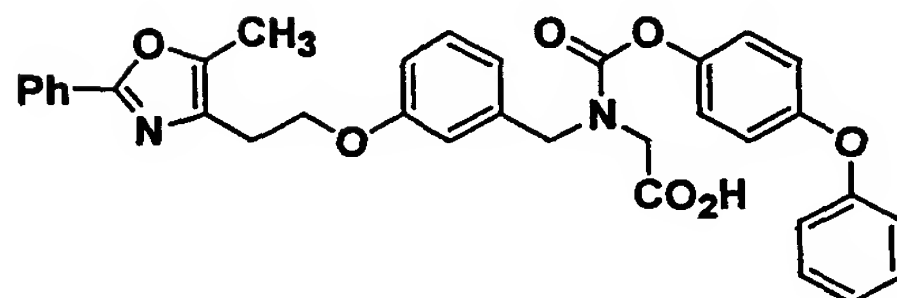
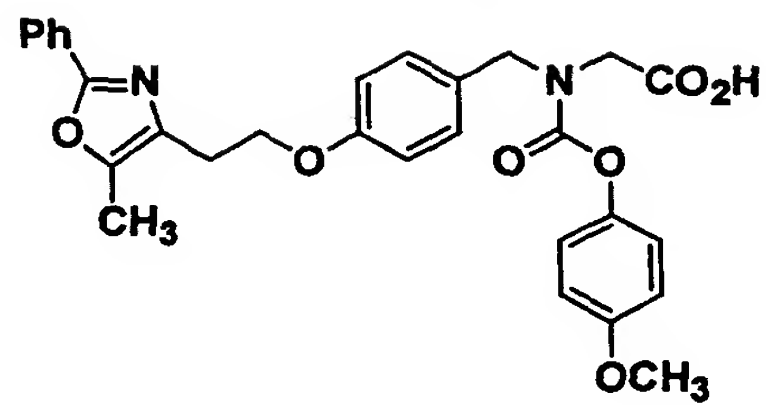


20. The compound as defined in Claim 1 having the structure



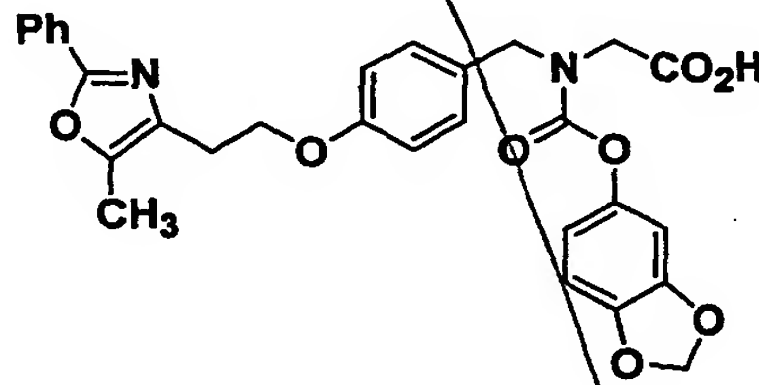
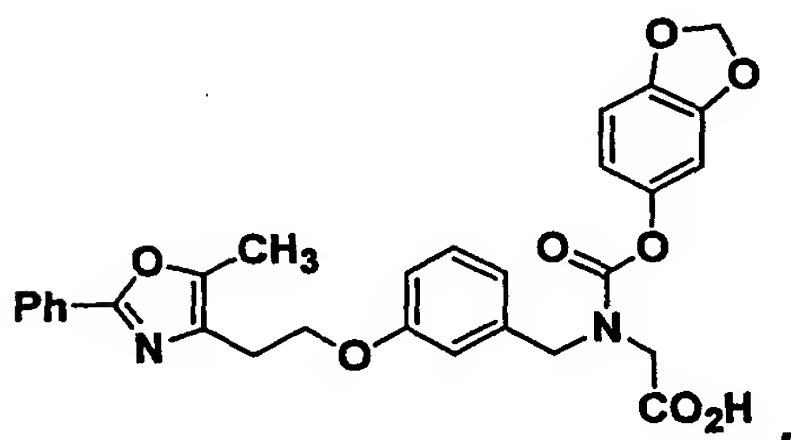
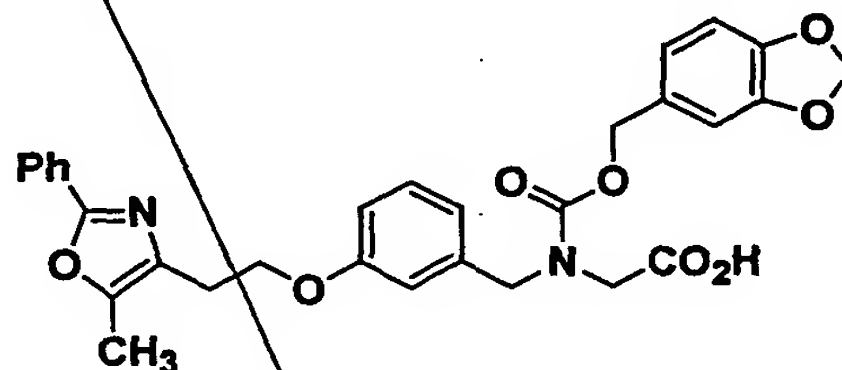
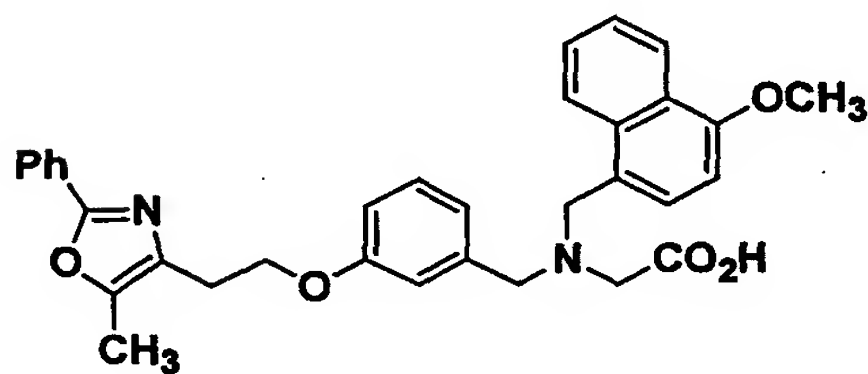
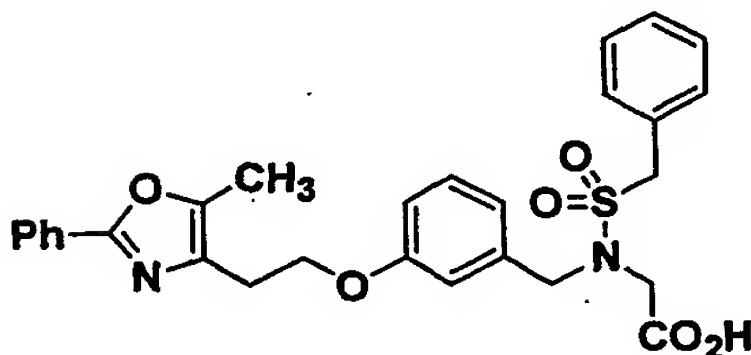
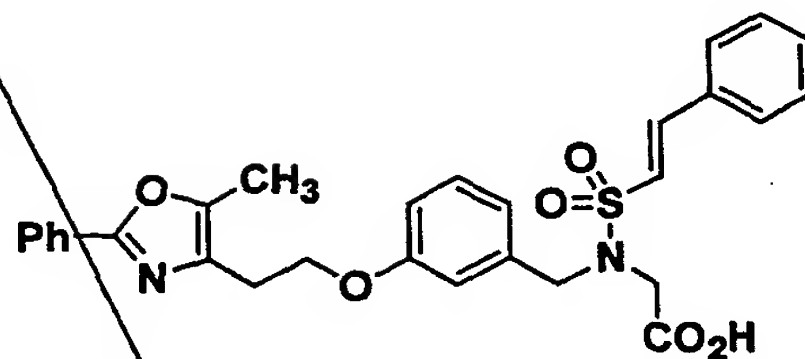
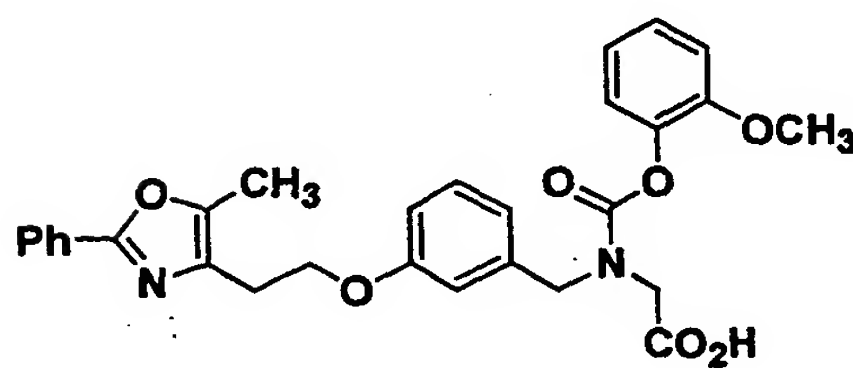
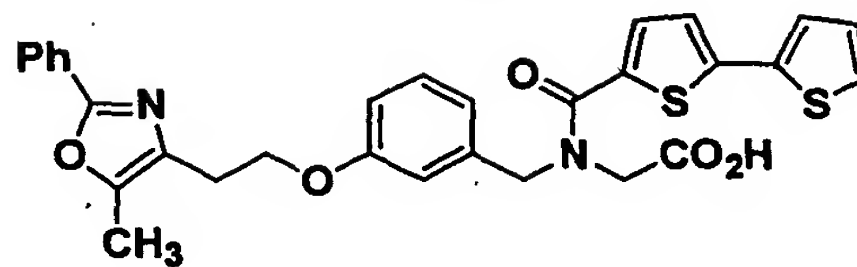
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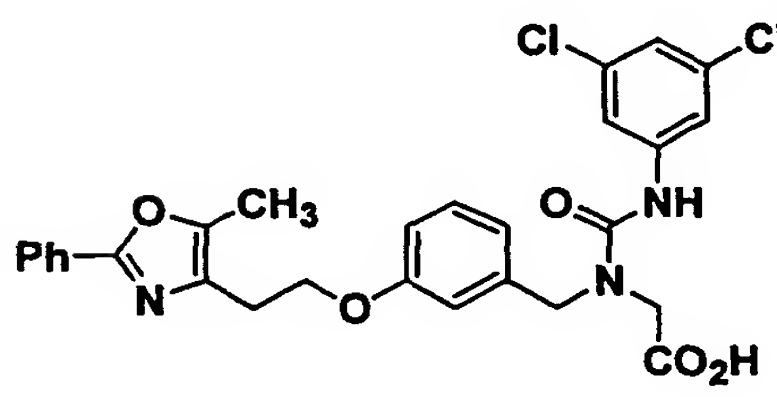
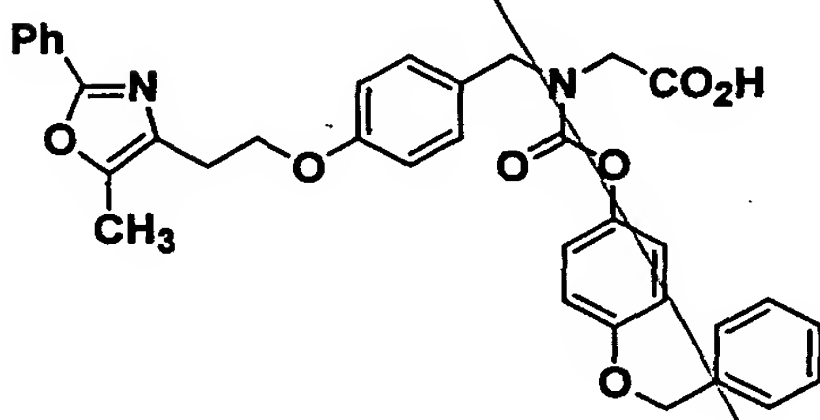
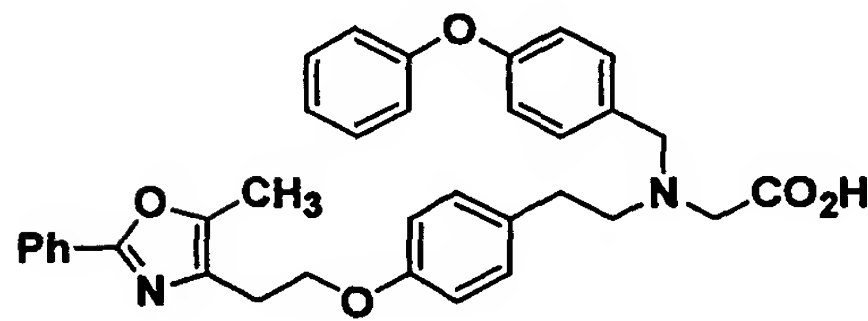
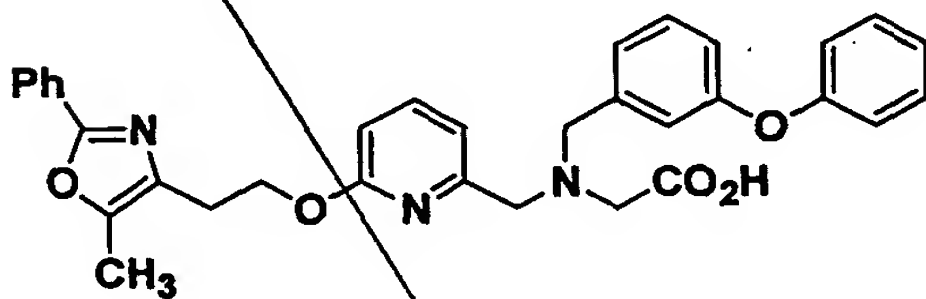
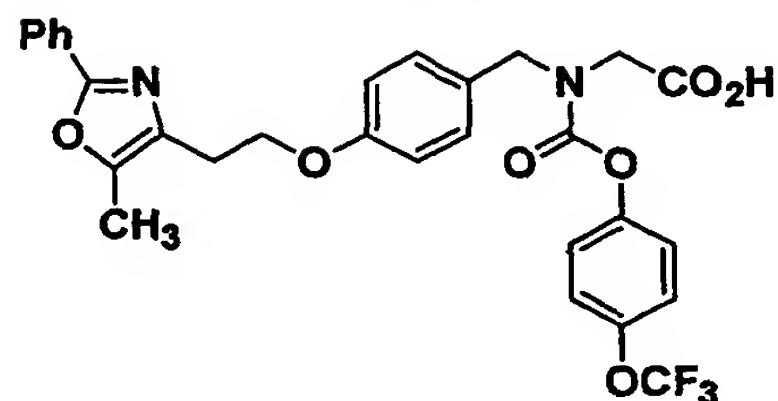
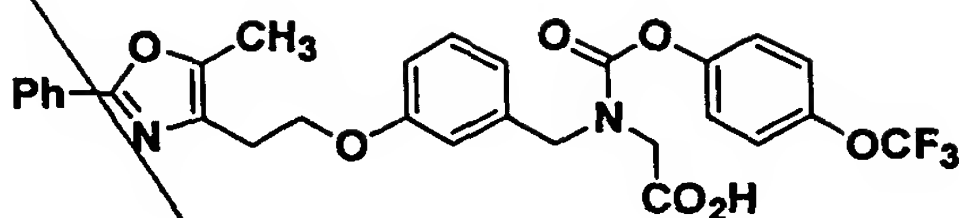


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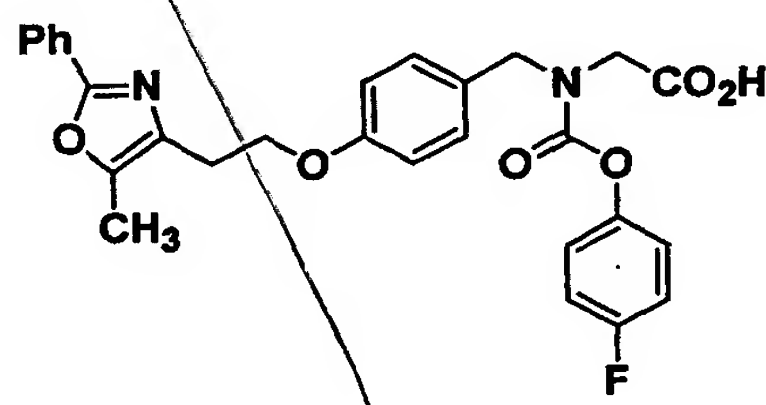
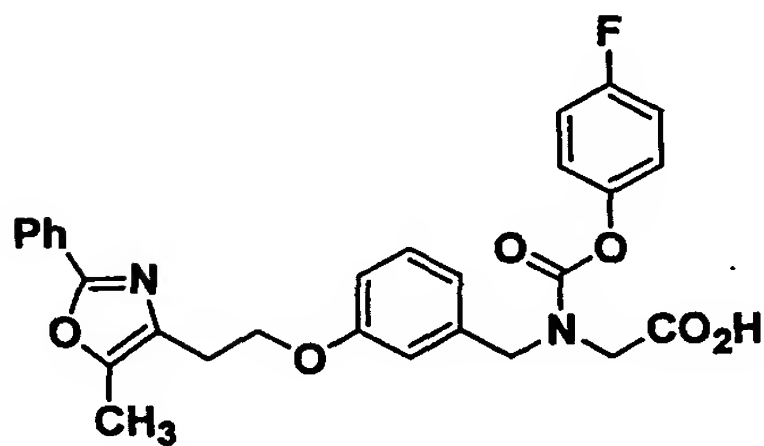
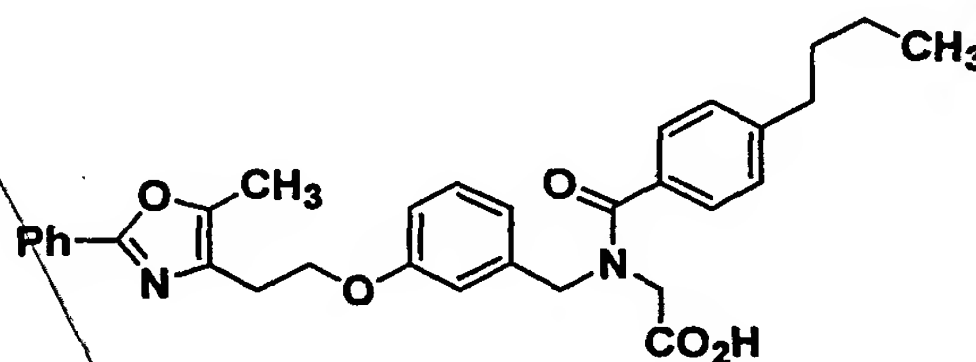
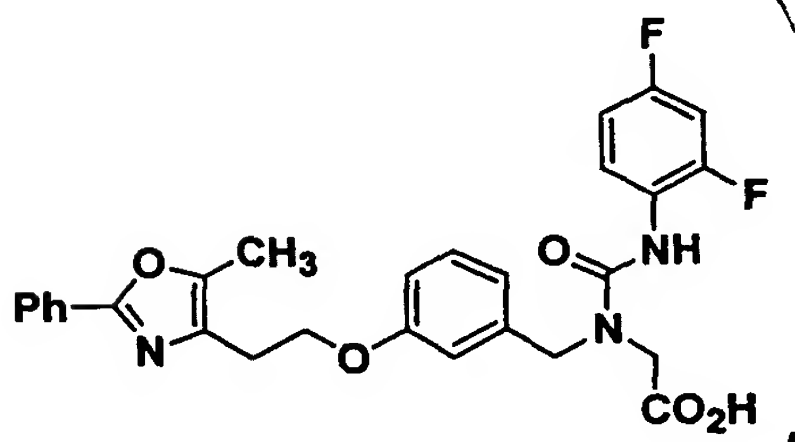
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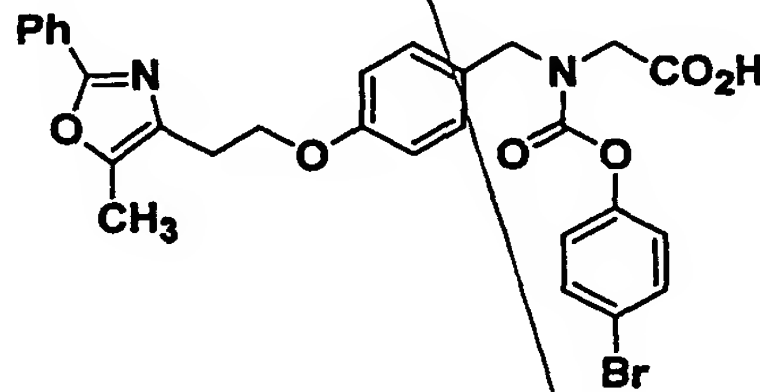
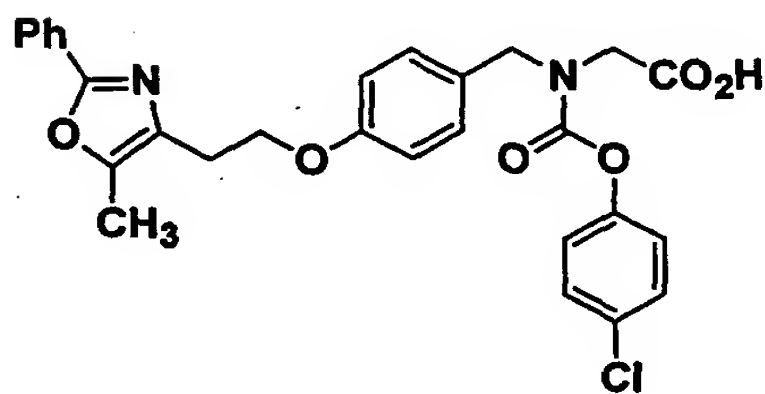
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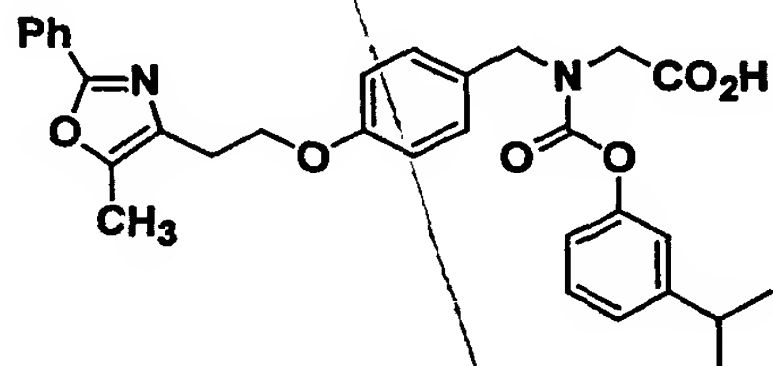
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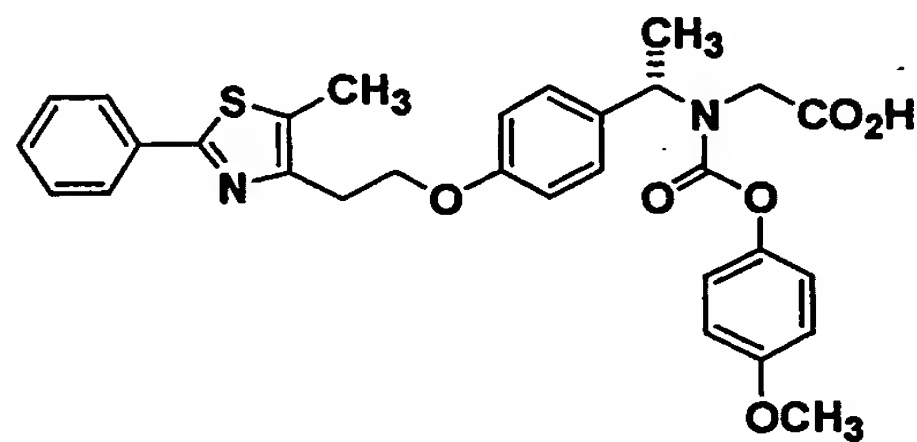
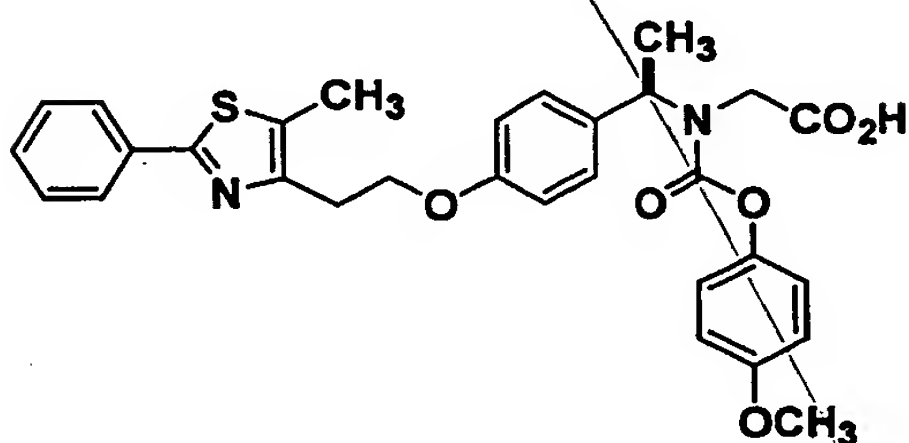
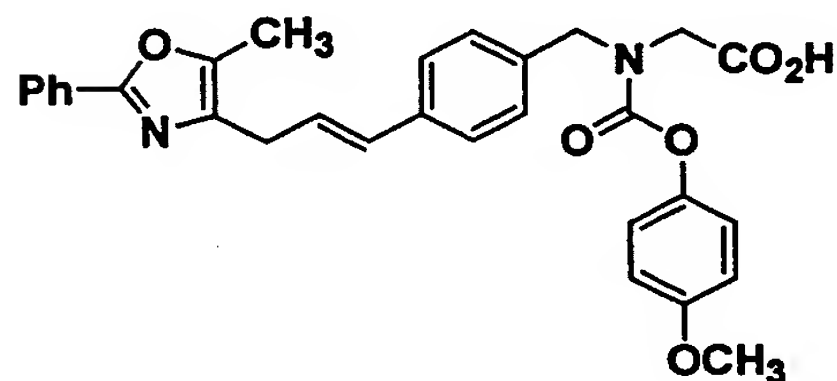
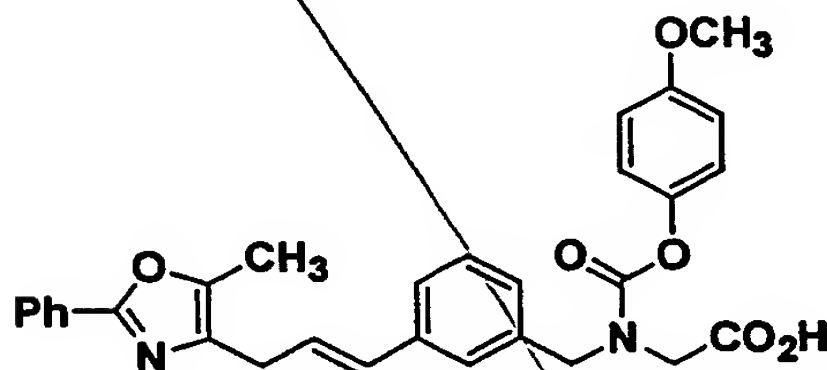
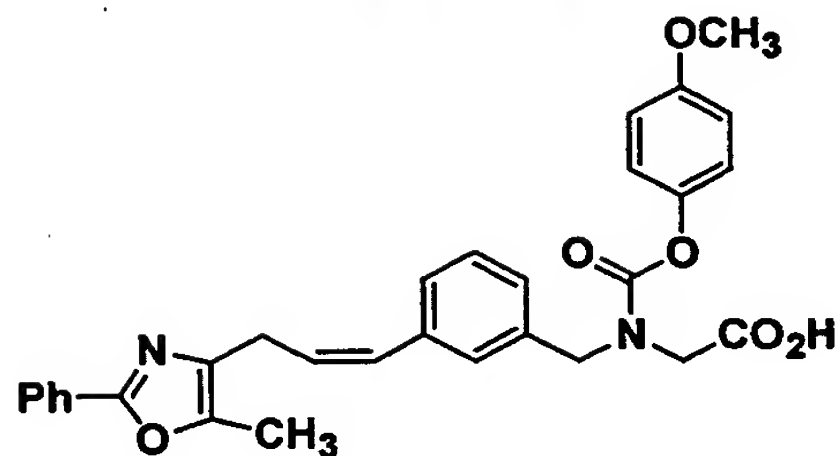
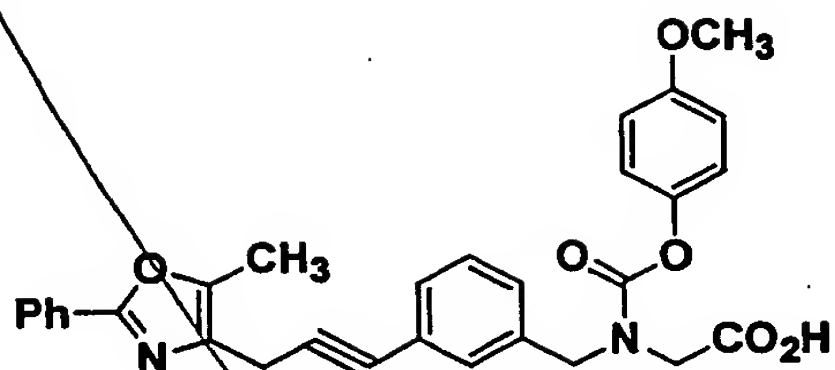
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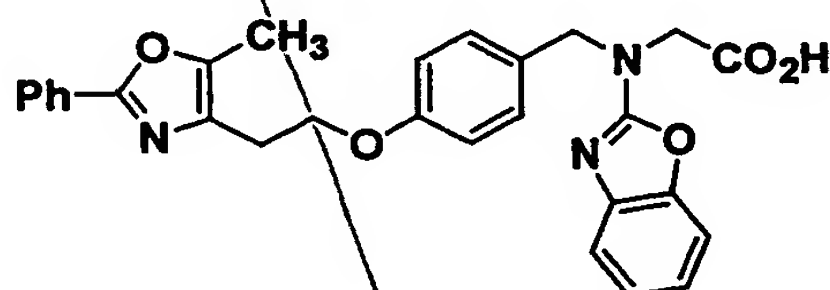
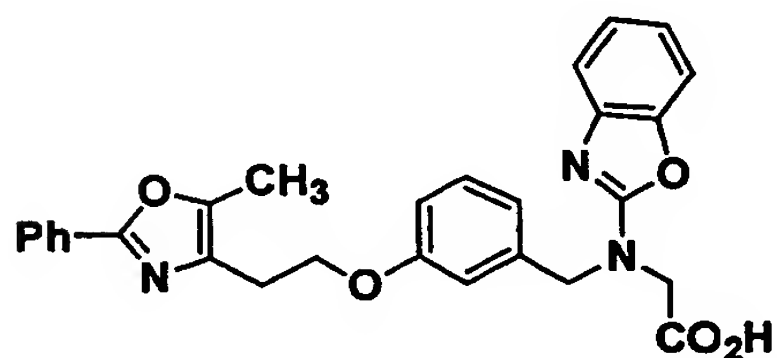
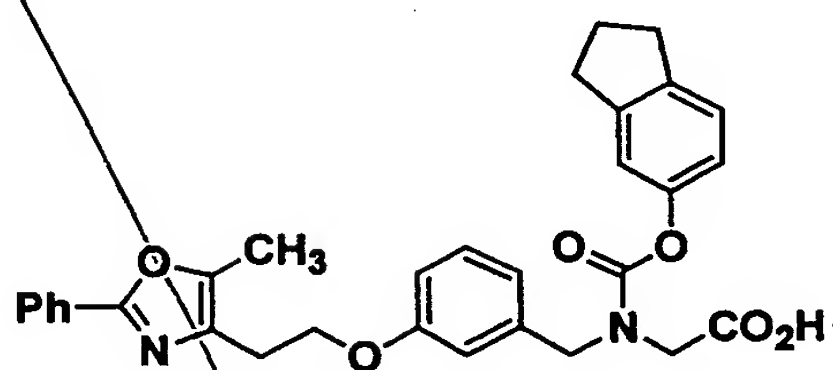
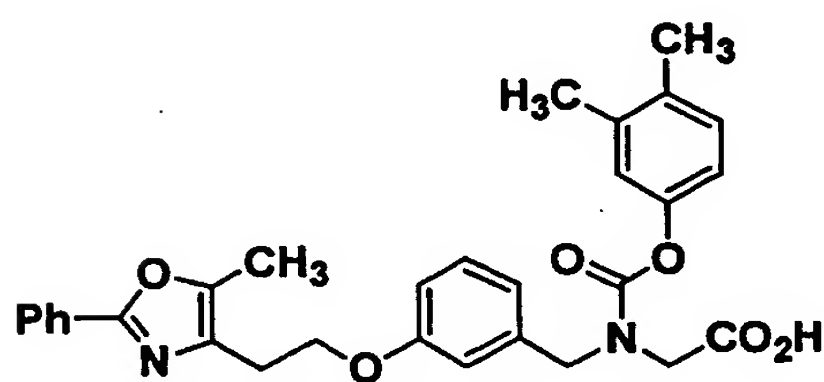
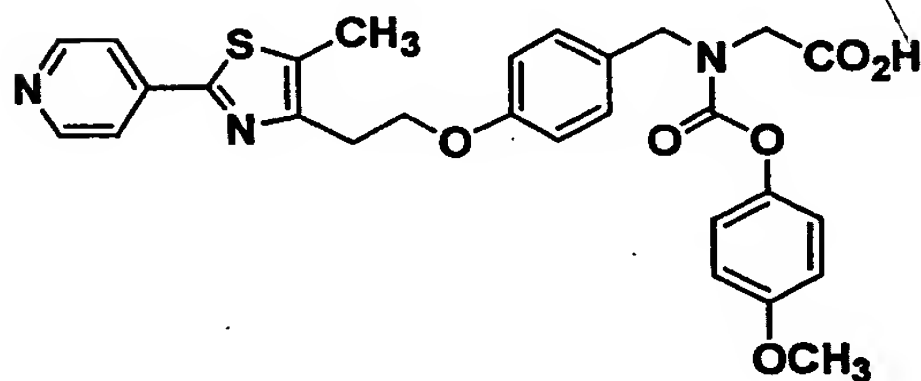
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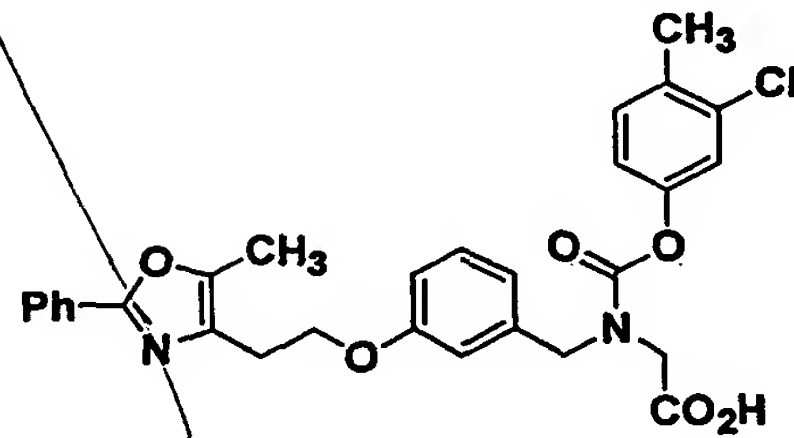
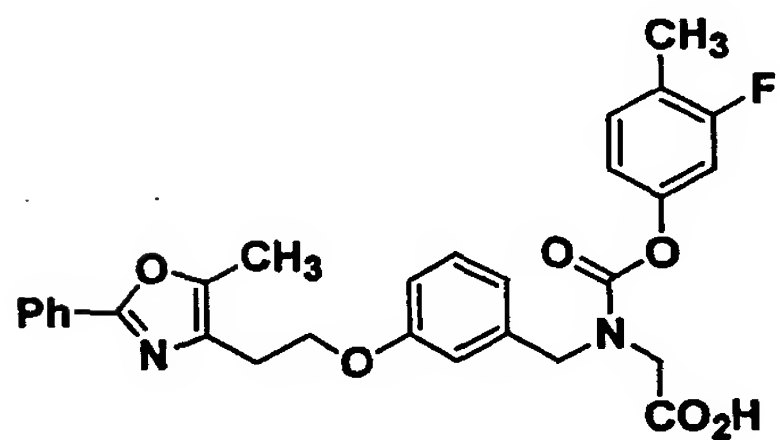
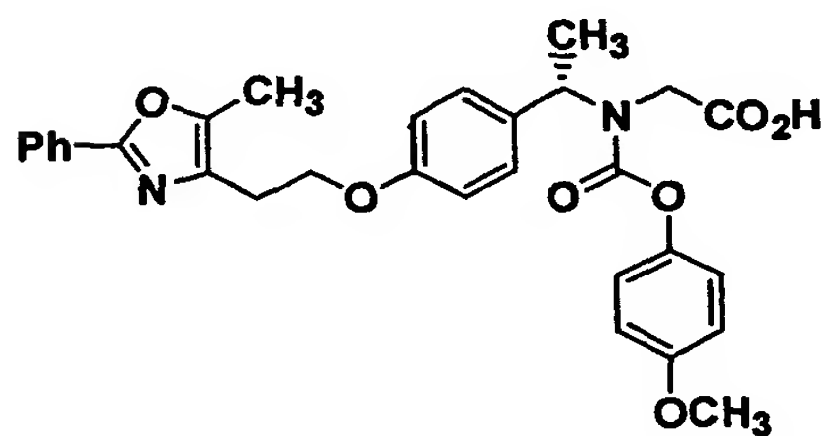
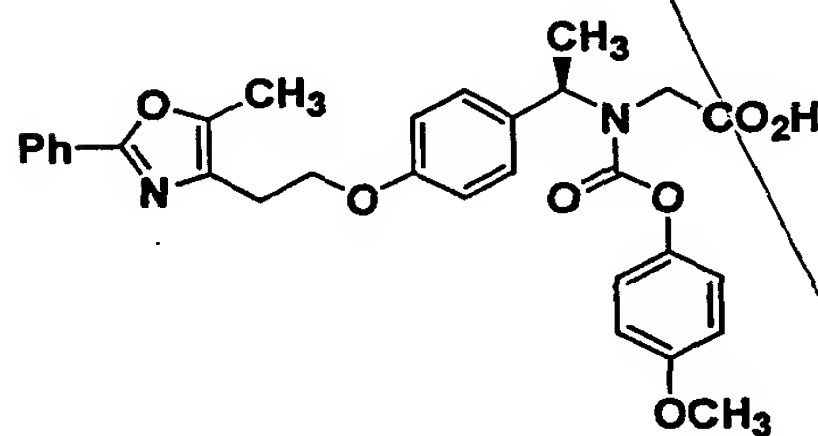
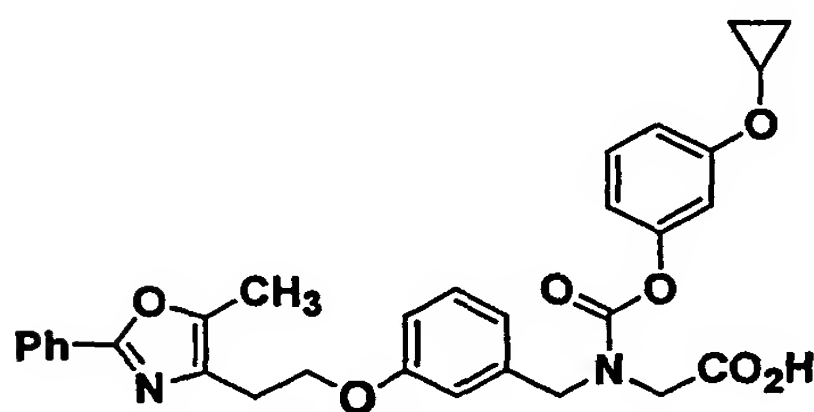
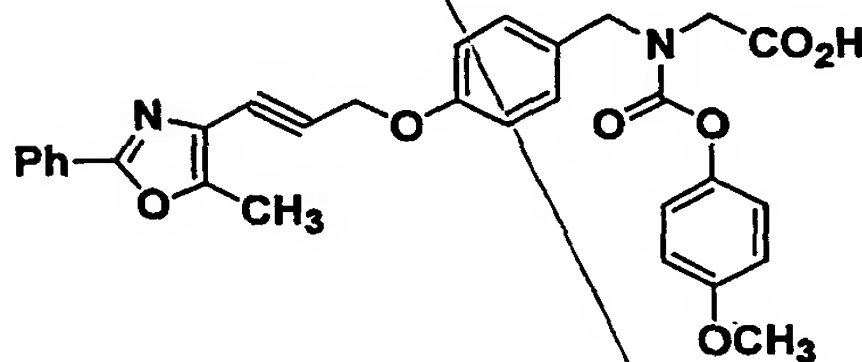
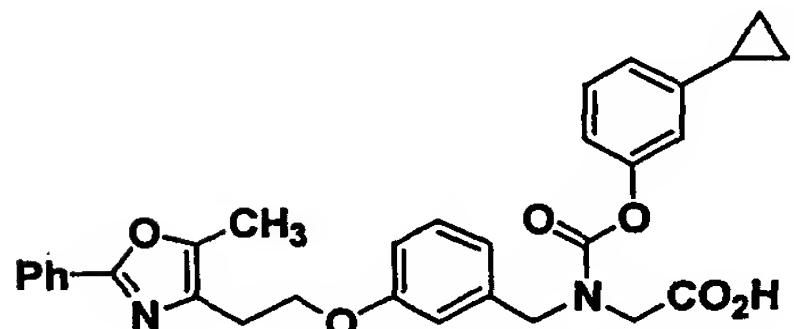
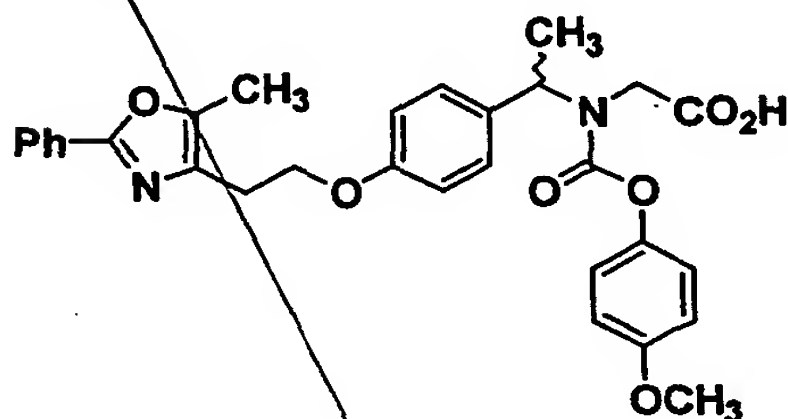
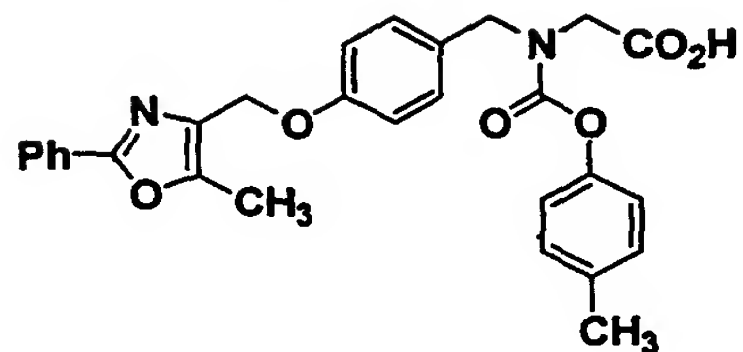
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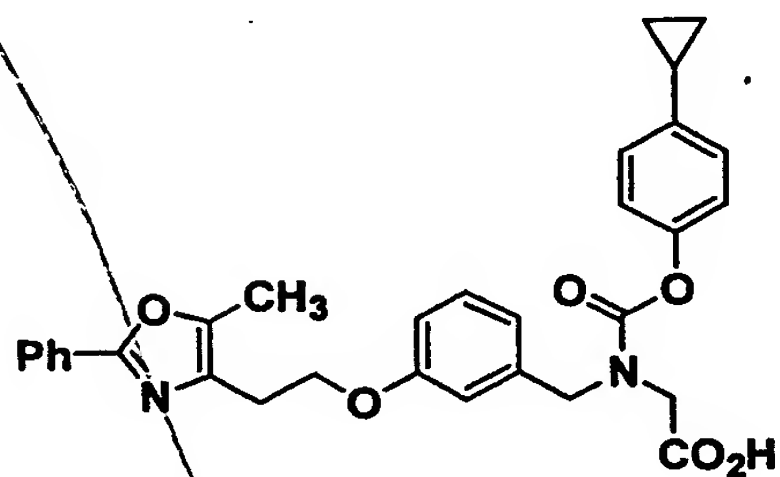
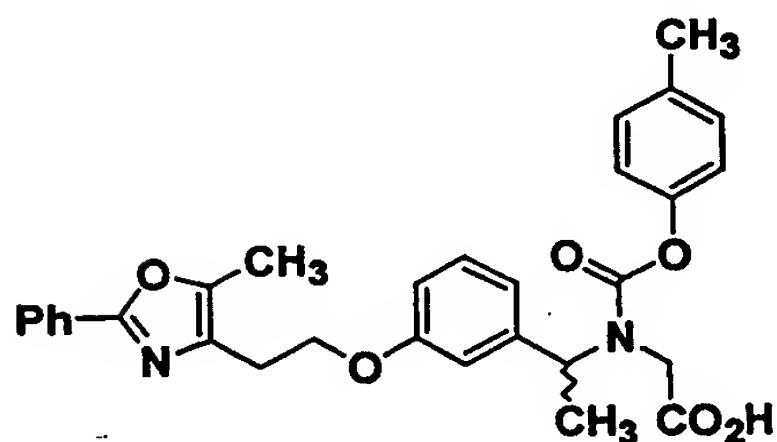
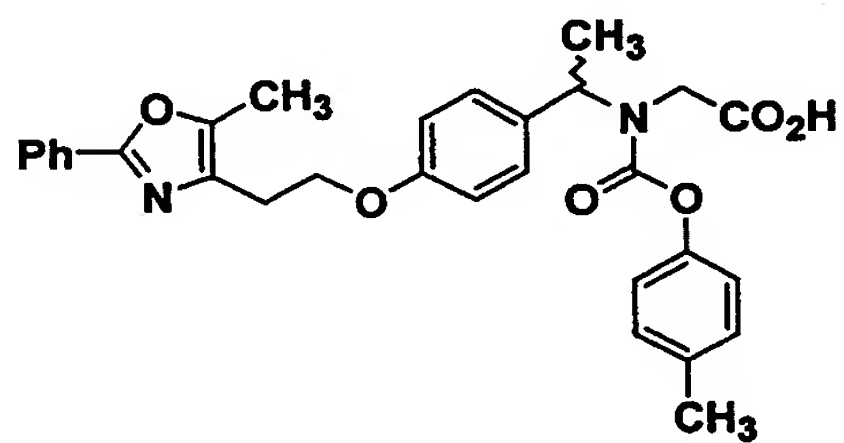
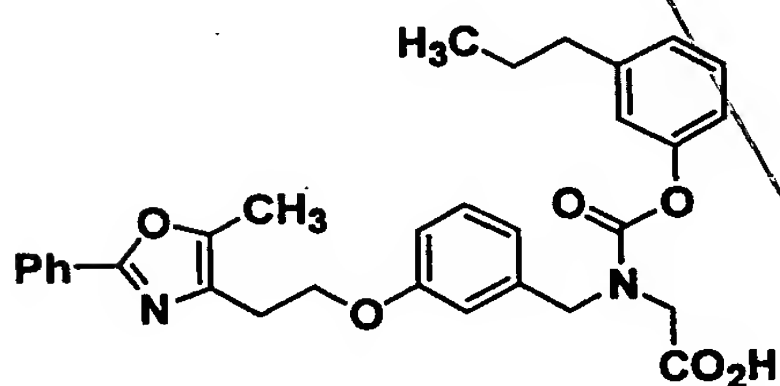
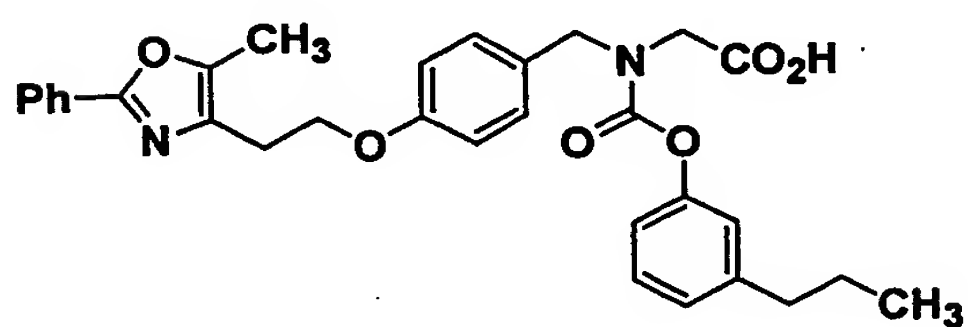
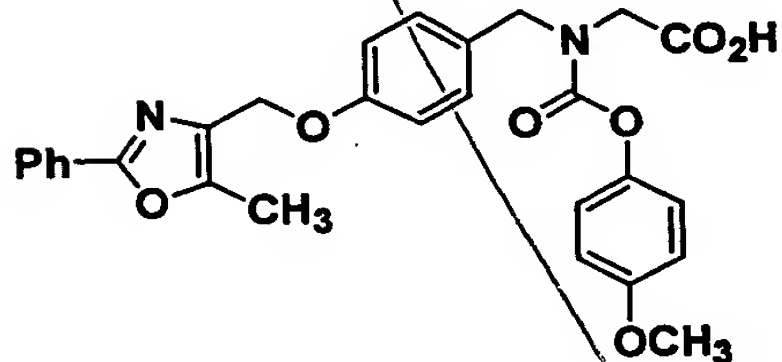
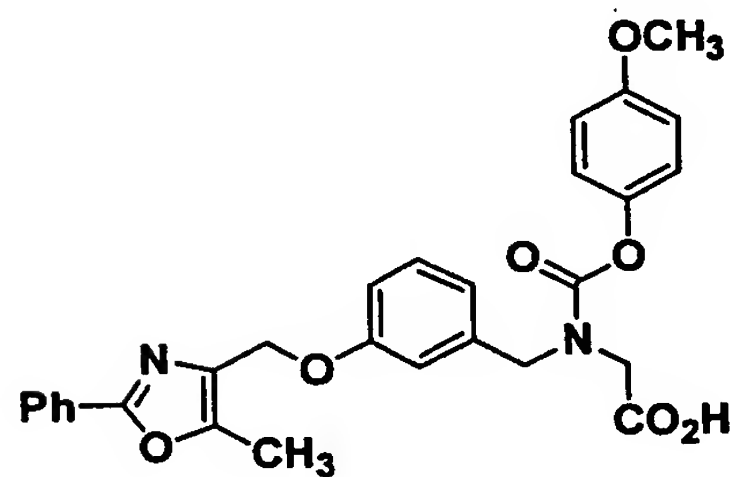
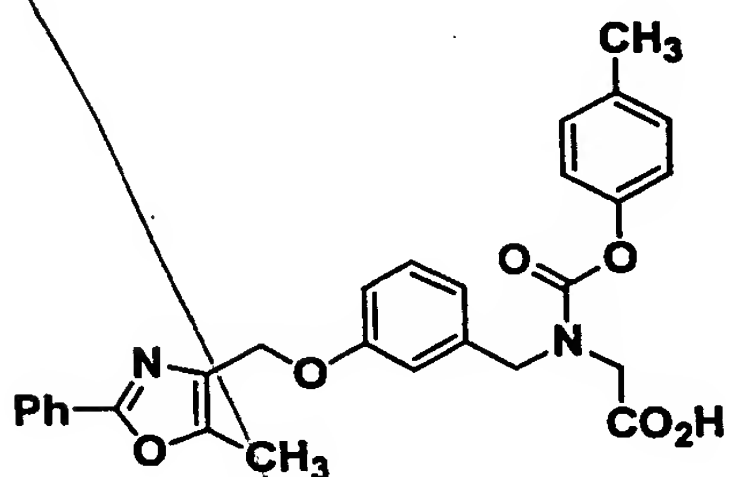
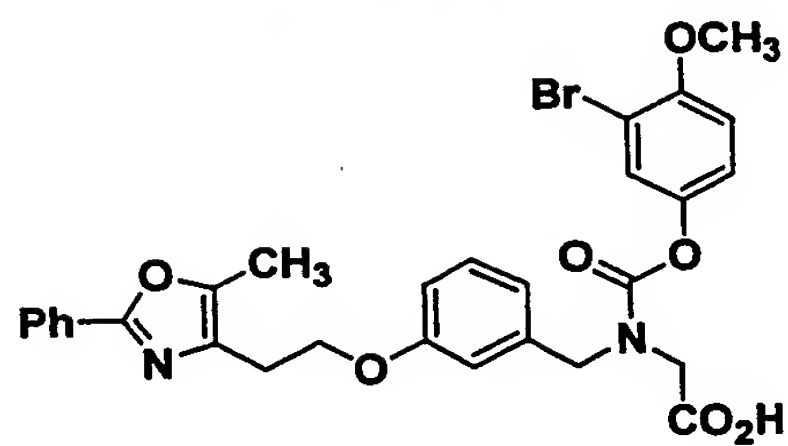
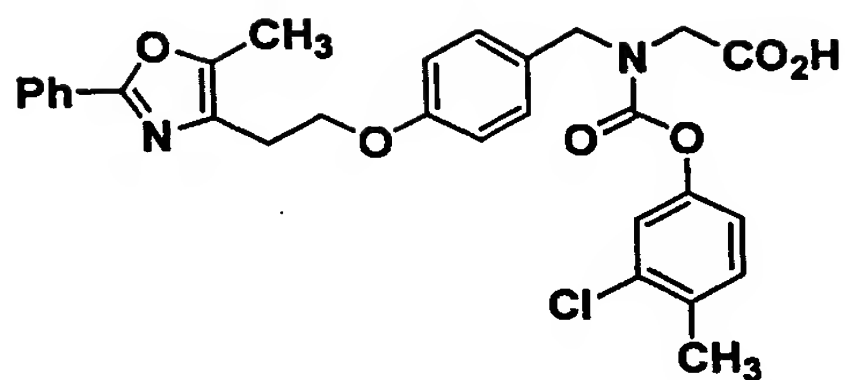


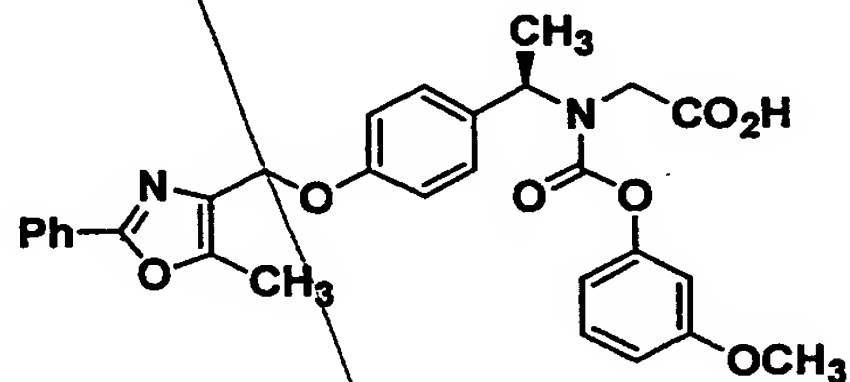
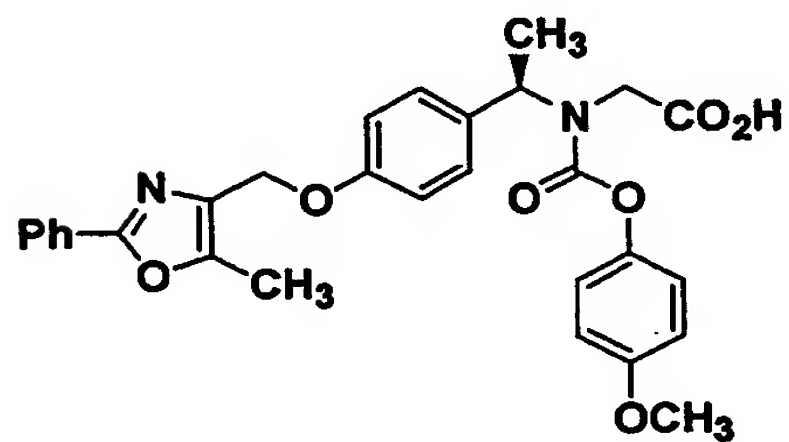
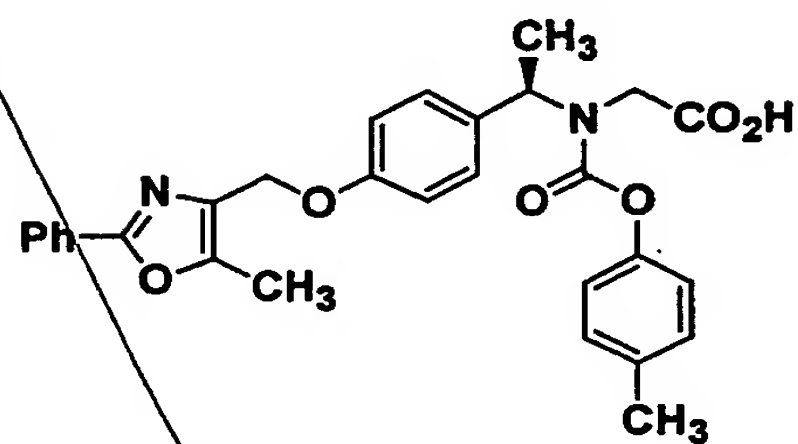
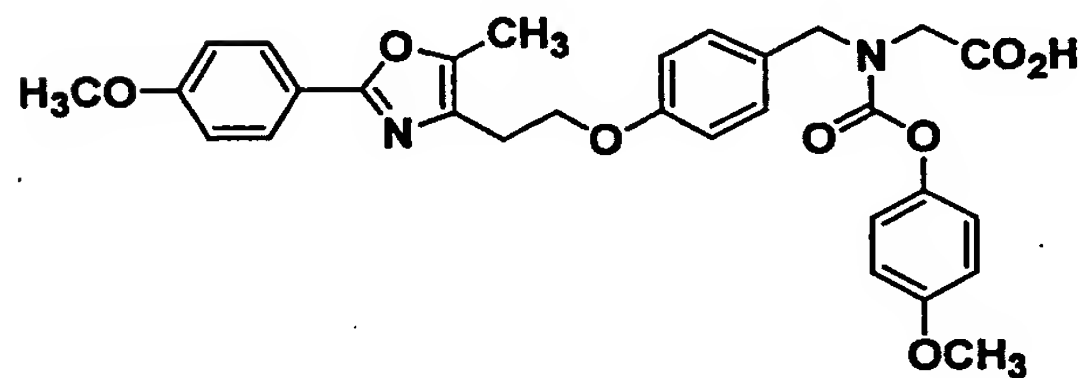
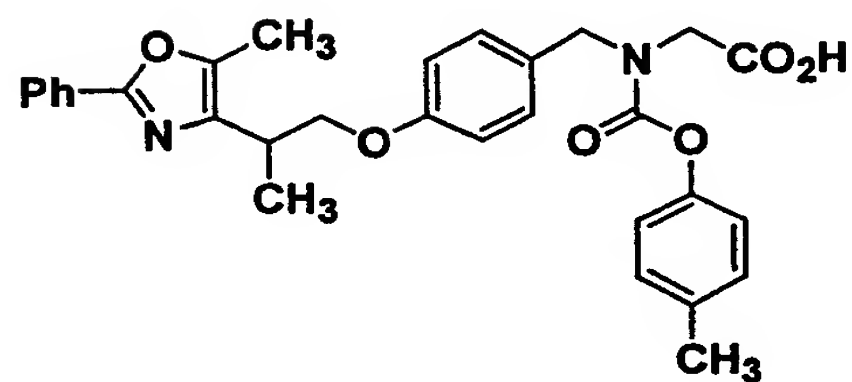
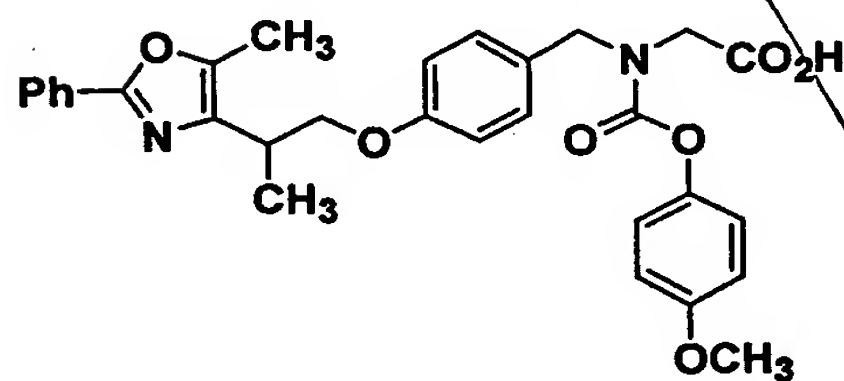
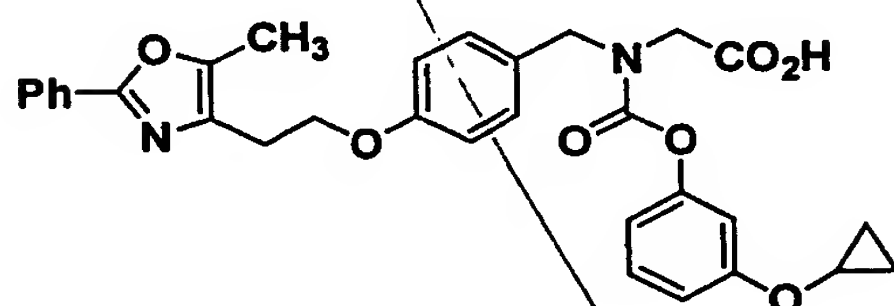
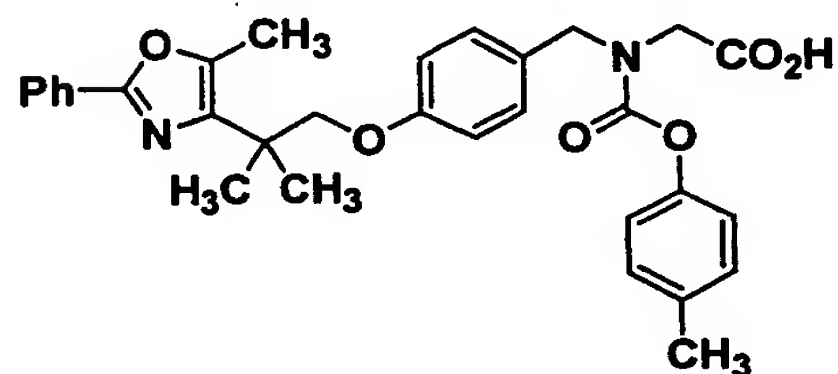
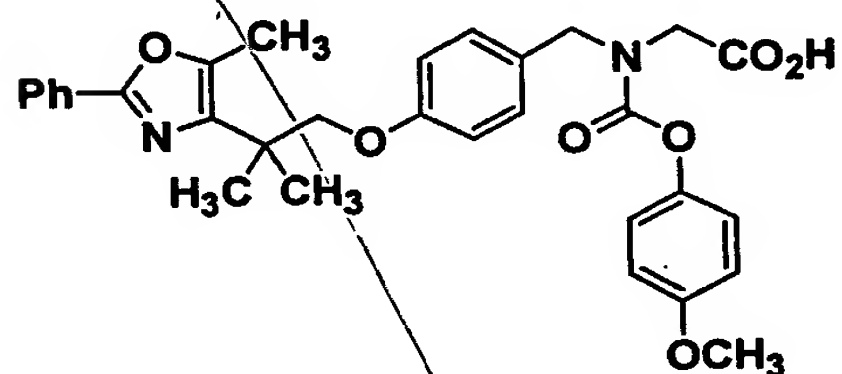
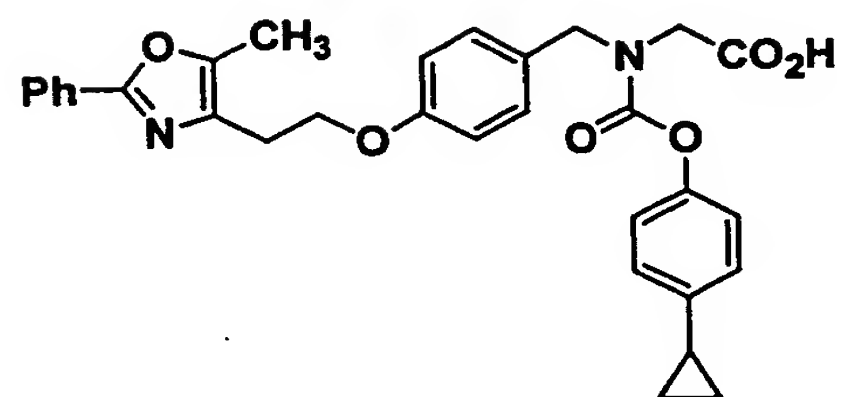
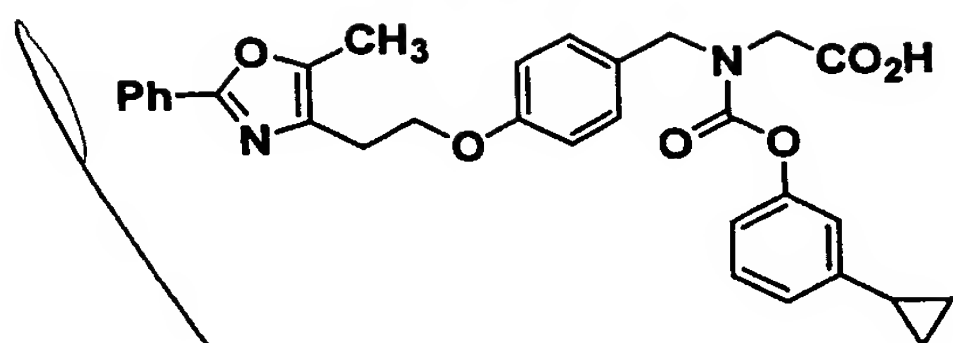
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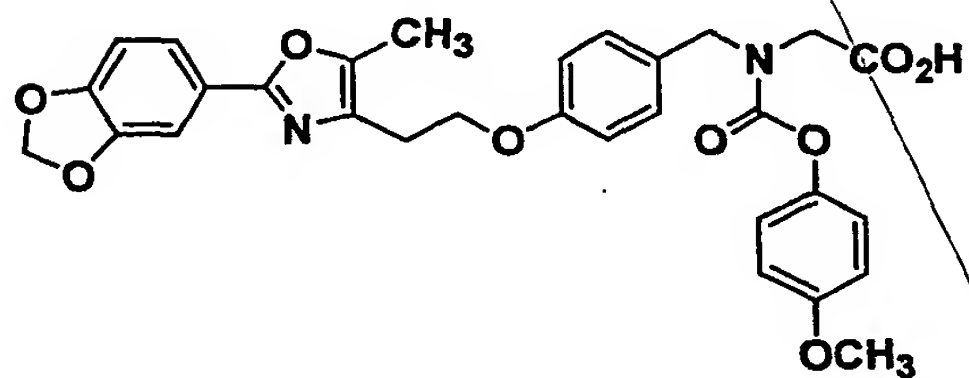
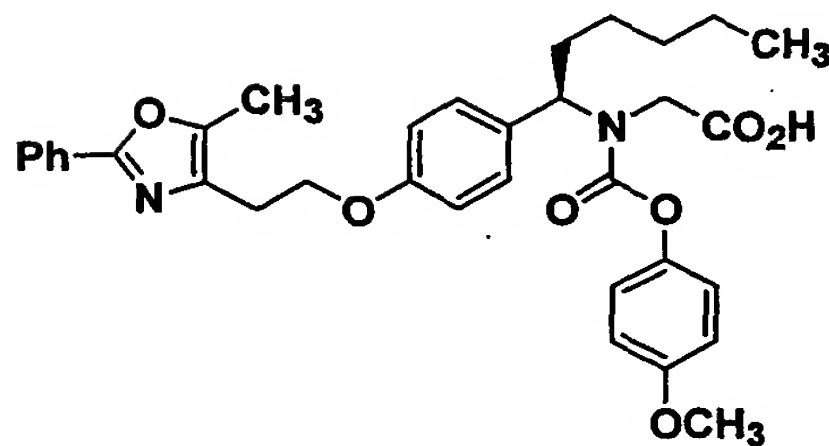
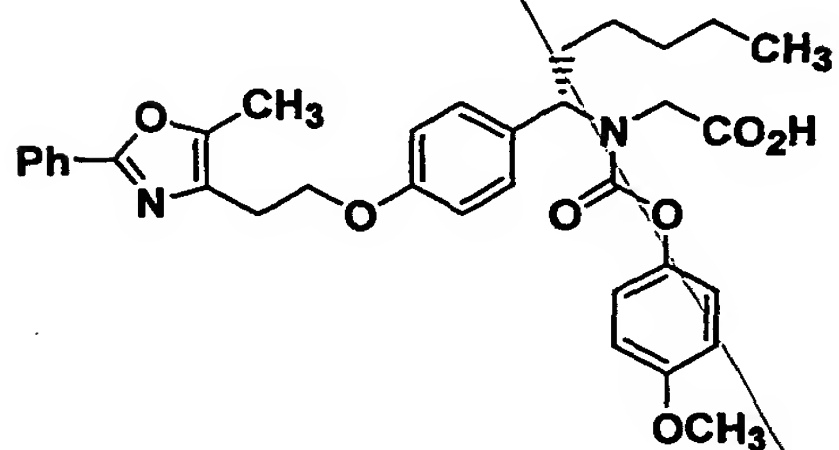
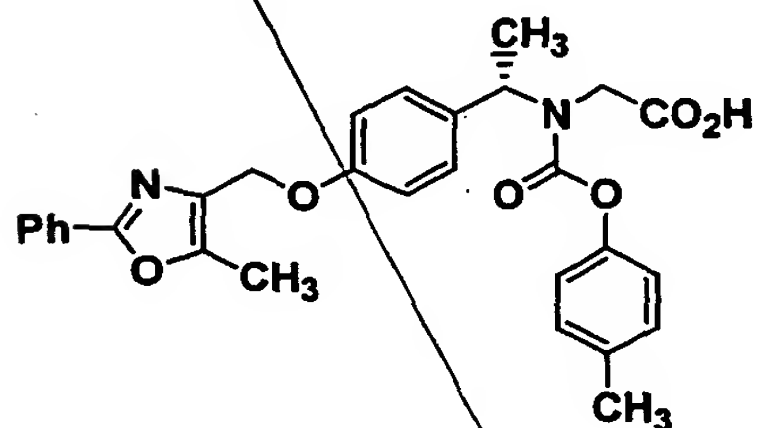
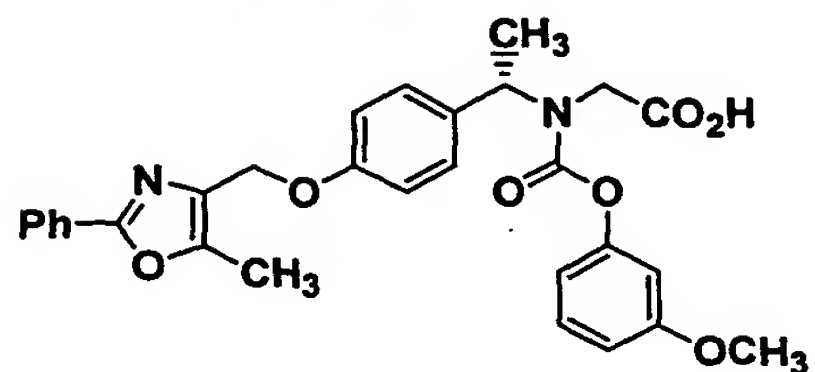
CC1=CC=C(C=C1)C2=C(C)OC(=N2)CCOCC3=CC=C(C=C3)OCC(=O)NCC(=O)OC4=CC=C(C=C4)C(F)=C(C)C

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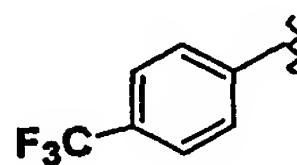
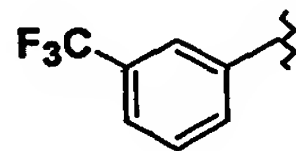
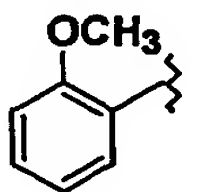
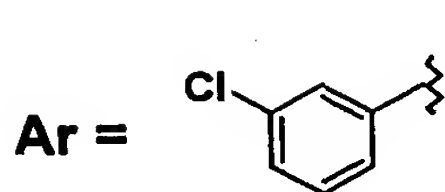
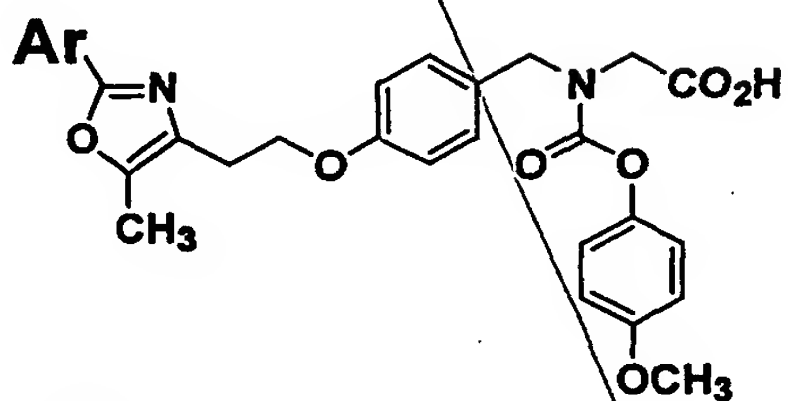
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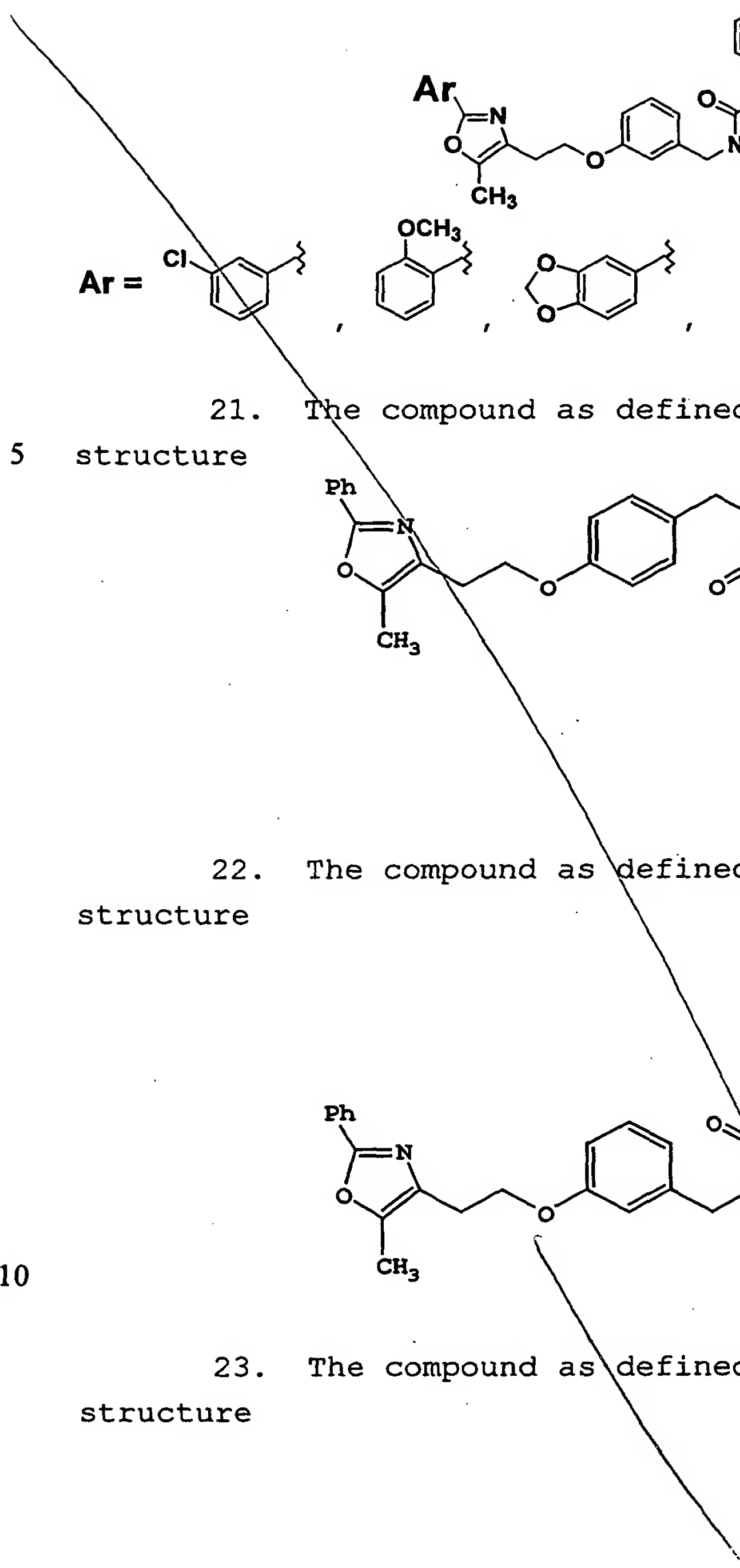




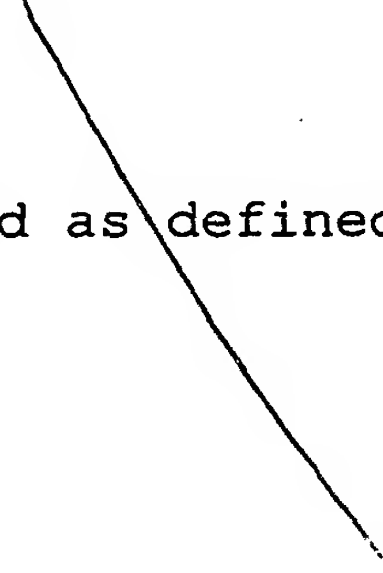


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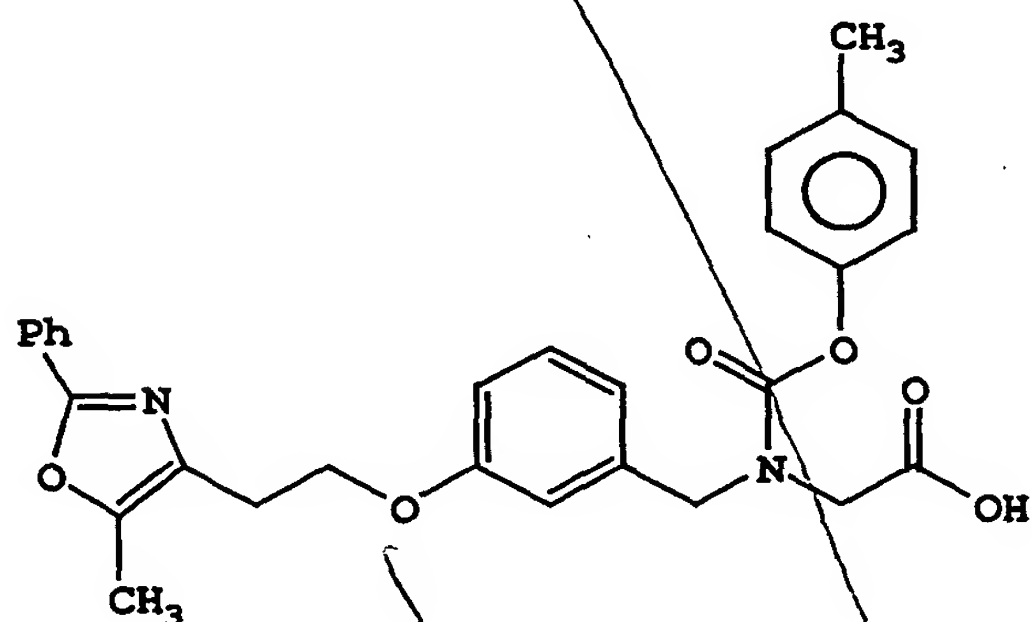




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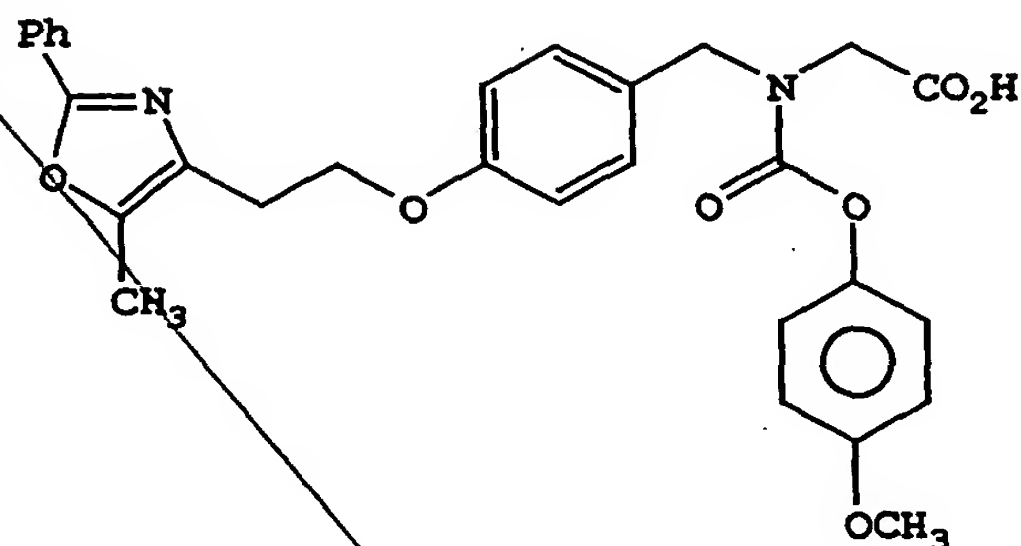


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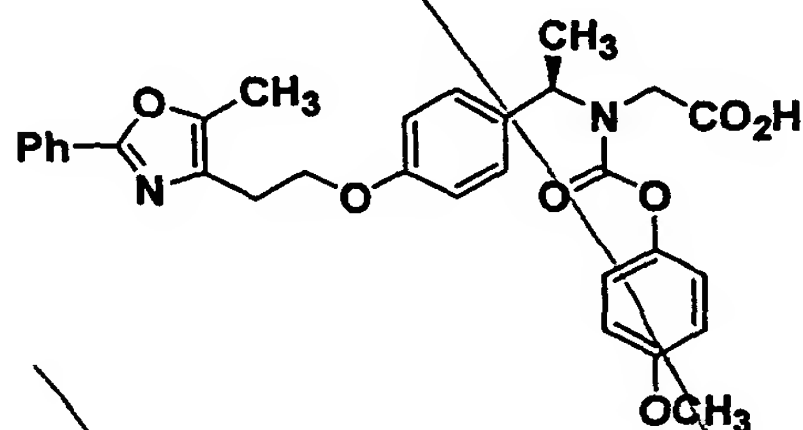


23. The compound as defined in Claim 1 having the structure

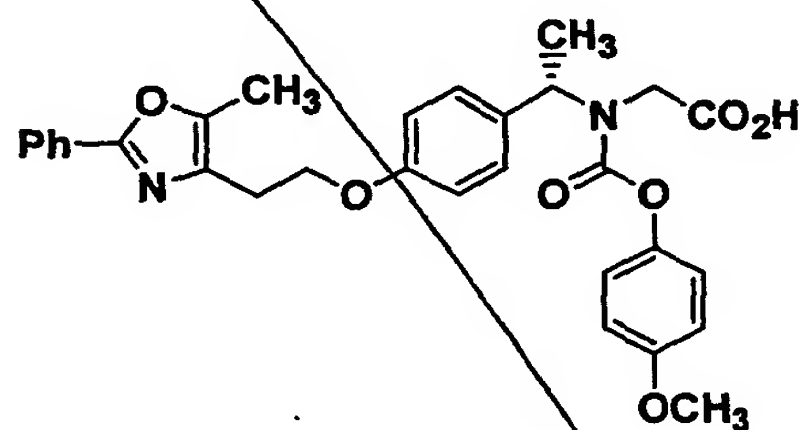
27. The compound as defined in Claim 1 having the structure



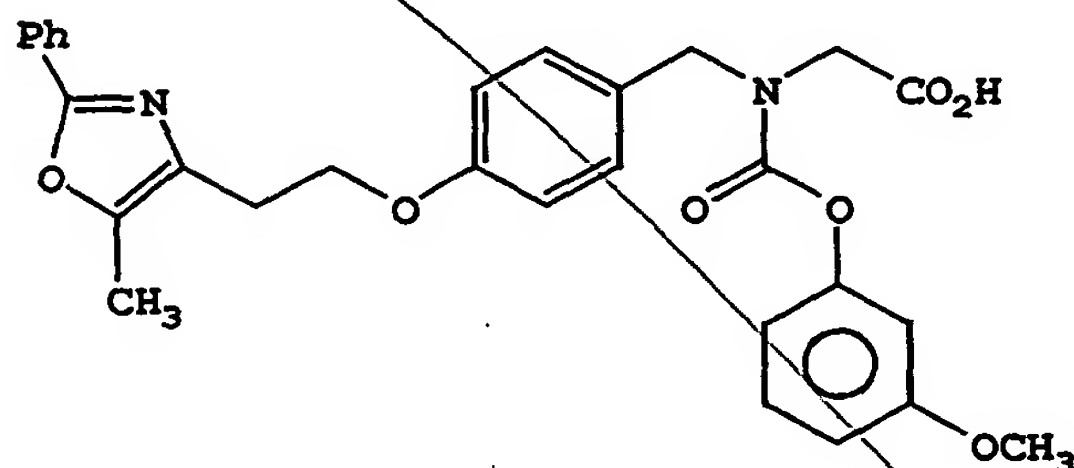
28. The compound as defined in Claim 1 having the structure



29. The compound as defined in Claim 1 having the structure



30. The compound as defined in Claim 1 having the structure



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Cont.

CC1=C(C(=C(C=C1)OC(=O)NCC(=O)O)C=C(C=C1)OCC2=C(C=C(C=C2)OC3=CC=CC=C3)N=C(N3)C=C(C)C=C3)C

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37. A pharmaceutical combination comprising a compound as defined in Claim 1 and a lipid-lowering agent, a lipid modulating agent, an antidiabetic agent, an anti-obesity agent, an antihypertensive agent, a platelet aggregation inhibitor, and/or an antiosteoporosis agent.

38. The pharmaceutical combination as defined in Claim 37 comprising said compound and an antidiabetic agent.

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39. The combination as defined in Claim 38 wherein the antidiabetic agent is 1, 2, 3 or more of a biguanide, a sulfonyl urea, a glucosidase inhibitor, a PPAR α agonist, a PPAR γ agonist, a PPAR α/γ dual agonist, an SGLT2 inhibitor, a DP4 inhibitor, an α P2 inhibitor, an insulin sensitizer, a glucagon-like peptide-1 (GLP-1), insulin and/or a meglitinide.

40. The combination as defined in Claim 39 wherein the antidiabetic agent is 1, 2, 3 or more of metformin, glyburide, glimepiride, glipyrider, glipizide, chlorpropamide, gliclazide, acarbose, miglitol, pioglitazone, troglitazone, rosiglitazone, insulin, Gl-262570, isaglitazone, JTT-501, NN-2344, L895645, YM-440, R-119702, AJ9677, repaglinide, nateglinide, KAD1129, AR-HO39242, GW-409544, KRP297, AC2993, LY315902, P32/98 and/or NVP-DPP-728A.

41. The combination as defined in Claim 38 wherein the compound is present in a weight ratio to the antidiabetic agent within the range from about 0.001 to about 100:1.

42. The combination as defined in Claim 37 wherein the anti-obesity agent is a beta 3 adrenergic agonist, a lipase inhibitor, a serotonin (and dopamine) reuptake

1. The first group of people who are not allowed to enter the country are those who are not citizens of the United States.

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[(2-mercapto-1-oxo-3-phenylpropyl) amino] -2,2-dimethyl-7-oxo-1H-azepine-1-acetic acid (gemopatrilat) or CGS 30440;
an angiotensin II receptor antagonist which is
irbesartan, losartan or valsartan;

5 amlodipine besylate, prazosin HCl, verapamil,
nifedipine, nadolol, propranolol, carvedilol, or
clonidine HCl.

49. The combination as defined in Claim 37 wherein
10 the platelet aggregation inhibitor is aspirin,
clopidogrel, ticlopidine, dipyridamole or ifetroban.

15 50. A method for treating insulin resistance,
hyperglycemia, hyperinsulinemia, or elevated blood levels
of free fatty acids or glycerol, hyperlipidemia, obesity,
Syndrome X, dysmetabolic syndrome, inflammation, diabetic
complications, impaired glucose homeostasis, impaired
glucose tolerance, hypertriglyceridemia or
20 atherosclerosis which comprises administering to a
mammalian species in need of treatment a therapeutically
effective amount of a pharmaceutical combination as
defined in Claim 43.

25 51. A method for treating irritable bowel syndrome, Crohn's disease, gastric ulceritis or osteroporosis, or psoriasis, which comprises administering to a mammalian species in need of treatment a therapeutically effective amount of a compound as defined in Claim 1.

52. The method as defined in Claim 36 wherein the disease is a liposarcoma or an epithelial tumor.

53. The method as defined in Claim 52 wherein the
35 epithelial tumor is a tumor of the breast, prostate,
colon, ovaries, stomach or lung.

54. The method as defined in Claim 36 wherein the disease is ductal carcinoma in situ of the breast, lobular carcinoma in situ of the breast, fibroadenoma of the breast, or prostatic intraepithelial neoplasia.

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add
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add B2